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DRUG EVALUATIONS

by the Council on Pharmacy and Chemistry of the American Medical Association

The following monographs and supplemental statements on drugs have been authorized by the Council on Pharmacy and Chemistry of the American Medical Association for publication and inclusion in *New and Nonofficial Remedies*. They are based upon the evaluation of available scientific data and reports of investigations.

Beginning with this issue, THE BULLETIN will carry these drug evaluations so that they will be more readily available to hospital pharmacists. This information should be of great use to the hospital pharmacist in his work with the Pharmacy and Therapeutics Committee and the medical staff. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Pharmacy and Chemistry; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of THE BULLETIN include those published in the *Journal* to April 1, 1956.

Notice of Change in Operation

Listing of Trade Names

The Council has adopted a revision of its Principles Governing the Evaluation of Drugs for Inclusion in New and Nonofficial Remedies (New Program of Operation for Evaluation of Drugs, *J.A.M.A.* **158:**1170 [July 30] 1955). The revision, effective Jan. 1, 1956, provides for listing names of marketed preparations of drugs in conjunction with individual monographs published in the Council's New and Nonofficial Remedies column and included in New and Nonofficial Remedies. It reads as follows:

The Council encourages the early adoption of a non-proprietary name for general use in identifying each drug. The Council believes that such names tend to diminish confusion. Each drug evaluated is described by a non-proprietary name; however, the Council recognizes the usefulness of the trademark for the physician who wishes to prescribe, or refer to, some particular brand.

Names for marketed preparations of individual drugs of which the Council has knowledge or is informed will be listed alphabetically in conjunction with each published monograph as a matter of information. Names or alterations in names of which the Council was not informed prior to initial publication of a monograph will be included in subsequent editions of New and Nonofficial Remedies upon receipt of such information.

J. Am. Med. Assoc. 160:50 (Jan. 7, 1956)

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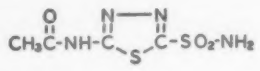
Acetazolamide — Diamox®

ACETAZOLAMIDE is 5-Acetamido-1,3,4-thiadiazole-2-sulfonamide.—The structural formula of acetazolamide may be represented as follows:



Actions and Uses

ACETAZOLAMIDE, a heterocyclic sulfonamide compound, is a potent inhibitor of carbonic anhydrase, the enzyme that catalyzes the reversible hydration of carbon dioxide and dehydration of carbonic acid. The most important pharmacological action of acetazolamide is referable to inhibition of carbonic anhydrase in the renal tubule resulting in a depression of tubular reabsorption of bicarbonate; however, the drug acts in a manner completely different from that of the organic mercurials, promoting the excretion of bicarbonate ion rather than chloride ion. The result of this selective action is loss from the extracellular fluid, by way of the kidney, of sodium bicarbonate, to a lesser extent of potassium bicarbonate, and of an isosmotic equivalent of water. Thus, diuresis, alkalinization of the urine, and a mild degree of metabolic acidosis occur.

Acetazolamide is absorbed rapidly from the gastrointestinal tract. Peak plasma levels are reached within 2 hours after administration, and the duration of therapeutic effectiveness is about 8 to 12 hours. The drug is rapidly excreted in an unchanged form by the kidney, about 80% of a single oral dose appearing in the urine within 8 to 12 hours.

Acetazolamide has been employed as a diuretic in the treatment of edema associated with congestive heart failure. Unlike most mercurials, it is well tolerated when given by the oral route, but its diuretic action is not as rapid or as dramatic as that observed after organic mercurial therapy. Patients with predominantly left-sided decompensation severe enough to require hospitalization usually do not respond well to therapy with this agent. In these patients, mobilization of pulmonary edema fluid is best achieved by use of the mercurials; however, subsequent replacement with acetazolamide may often maintain such patients in an edema-free state, with relief from dyspnea and orthopnea. In patients with severe right-sided heart failure and large accumulations of fluid, paracentesis is generally required before favorable responses to acetazolamide can be elicited. Here too, it is frequently necessary to initiate diuretic therapy with the mercurials, with subsequent replacement by acetazolamide.

The best results with this drug have been obtained in ambulatory patients with mild to moderate cardiac decompensation and cor pulmonale. Its use does not eliminate the need for other therapy such as with digitalis, bed rest, fluid restriction, or sodium-free diet. It is of no value in the treatment of nephrotic edema or nephritis.

Acetazolamide has been employed in the treatment of epilepsy. It is not known whether beneficial effects result from the systemic acidosis that the drug produces or from direct inhibition of brain carbonic anhydrase. Preliminary clinical investigations indicate that administration of the drug, alone or in conjunction with other therapy, is moderately successful in controlling seizures in selected cases of petit mal and grand mal epilepsy refractory to other forms of therapy. Since the response to the drug is inconsistent, it is difficult to determine which patients will respond favorably to therapy; therefore, its ultimate usefulness in the treatment of this condition remains to be determined.

Acetazolamide appears to have therapeutic value in the treatment of glaucoma. Its action is different from that of the usual miotics, since the drug depresses the formation of the aqueous humor rather than facilitates its drainage; it is therefore most valuable as a supplement to the therapy with cholinergics generally used to reduce intraocular pressure. The effects of prolonged therapy with acetazolamide are not conclusive, and long-term therapy requires careful selection of patients and careful observation while they are receiving the drug. With short-term therapy, the drug has proved useful in reducing intraocular pressure in patients in whom the standard miotics have been unsuccessful. In severe acute cases, acetazolamide is particularly helpful in permitting the ophthalmologist to temporize and to evaluate the situation more carefully before undertaking surgery.

Undesirable side-effects of acetazolamide therapy, though rather frequent, are usually not serious and are rapidly reversible. Drowsiness and paresthesias over the face and extremities are the most commonly encountered side-effects. Fatigue, excitement, gastrointestinal upsets, and polydipsia have been observed less frequently. In patients with hepatic cirrhosis, the drug may induce episodes of disorientation. Since acetazolamide is rapidly excreted, the inhibition of carbonic anhydrase by daily oral doses is intermittent, and compensatory mechanisms prevent serious distortions of acid-base balance; however, it is contraindicated in idiopathic renal hyperchloremic acidosis. Because the drug causes a sodium and potassium diuresis, it is also contraindicated in all conditions in which there is a known depletion of these ions, including adrenal cortical hypofunction (Addison's disease) or all types of adrenal failure. Since acetazolamide is a sulfonamide derivative, it is possible that any of the untoward reactions reported after bacteriostatic sulfonamide administration could occur after acetazolamide therapy. Fever and allergic type skin eruptions have already been reported in patients receiving this drug. Although other manifestations of sulfonamide reactions such as bone marrow depression, crystalluria, and renal calculi have not been observed, the physician should be alert for the appearance of such reactions, and the drug should be withdrawn at the first sign of their occurrence.

Dosage

Acetazolamide is administered orally. For diuresis in patients with congestive heart failure, 0.25 to 0.375 gm. daily in the morning appears to be the optimal dosage, although some may respond to administration every other day. Increasing the dosage beyond this level does not increase the diuresis and may increase the incidence of side-reactions. If diminished diuretic effectiveness occurs after prolonged administration, dosage adjustments may be necessary. In the treatment of epilepsy, the dosage must be individualized according to the response of the patient. Although some patients are reported to respond to lower doses, the proposed range is 0.375 to 1 gm. once a day. If the drug is administered adjunctively with other anticonvulsants, the initial daily dose should not exceed 0.25 gm. This can then be increased gradually. In the treatment of acute congestive and secondary glaucoma, acetazolamide should be used as an adjunct to the usual miotic therapy in doses of 0.25 gm. every 4 hours.

Preparations for use as stated for the foregoing drug are marketed under the following name: Diamox.

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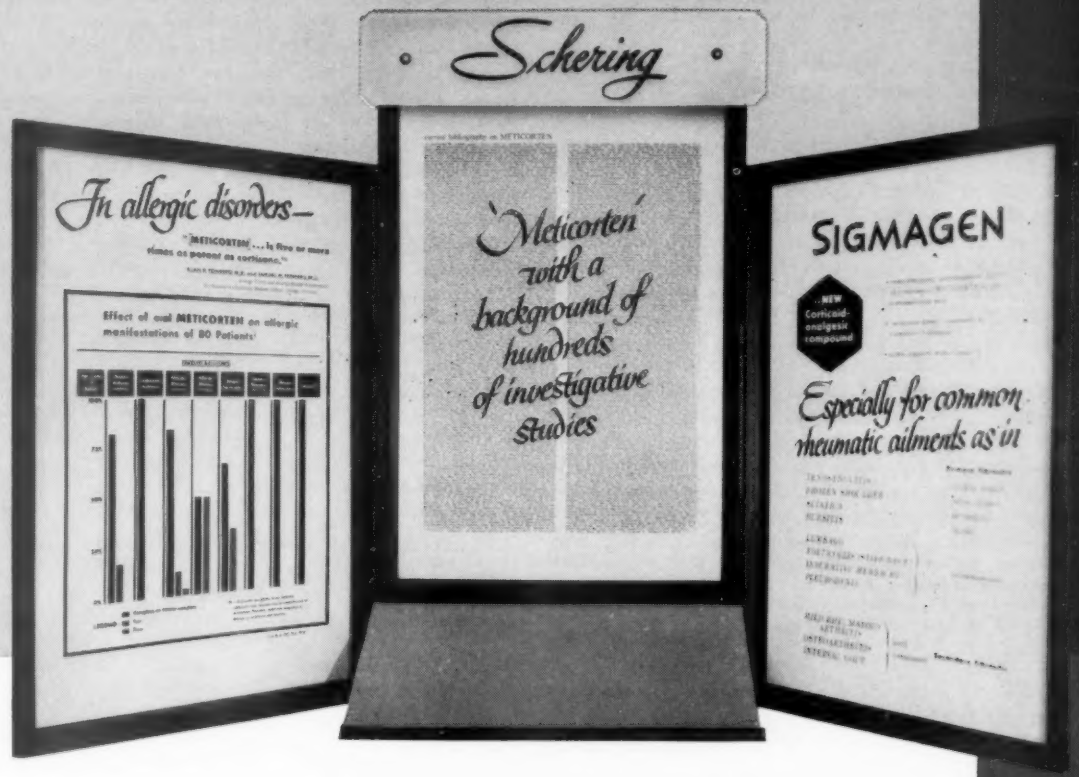
the first of a series of new hospital exhibits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'Meticorten' with a background of hundreds of investigative studies
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...NEW Corticoid-analgesic compound
Especially for common rheumatic ailments as in

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METICORTEN,* brand of prednisone.

*T.M.

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SCHERING

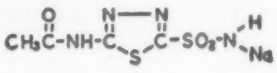
Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of acetazolamide.
—*J. Am. Med. Assoc.* *160*:1142 (Mar. 31, 1956)

Preparations

Tablets Acetazolamide (Diamox) 0.25 Gm., scored.

Acetazolamide Sodium — Diamox® Sodium

ACETAZOLAMIDE SODIUM is Sodium 5-acetamido-1, 3,4-thiadiazole-2-sulfonamide.—The structural formula of acetazolamide sodium may be represented as follows:



Actions and Uses

Acetazolamide sodium, the sodium salt of acetazolamide, exhibits the same actions and has the same potency as equivalent amounts of acetazolamide. It is more soluble than the parent drug and may therefore be administered parenterally. (See the monograph on acetazolamide.)

Dosage

Acetazolamide sodium is administered by either the intramuscular or intravenous routes. It should be given only when oral administration of acetazolamide is impractical. The dosage, expressed in terms of the parent drug, is the same as for acetazolamide. (See the monograph on acetazolamide.)

Preparations for use as stated for the foregoing drug are marketed under the following name: Diamox Sodium.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of acetazolamide sodium.
—*J. Am. Med. Assoc.* *160*:1143 (Mar. 31, 1956)

Preparations

Injection Acetazolamide (Diamox) Sodium 0.5 Gm., dry.

Antihistaminics — Injectable Antihistaminics For Prevention and Treatment of Transfusion Reactions

The Council has been requested to evaluate the effectiveness of several injectable antihistaminic drugs that have been used for the prevention and treatment of blood transfusion reactions. These include solutions for injection of chlorpheniramine maleate, diphenhydramine hydrochloride, methapyrilene hydrochloride, and tripelennamine hydrochloride. On the basis of currently available evidence, the Council concluded that these agents are capable of ameliorating, although not preventing, the severity of nonhemolytic, nonpyrogenic transfusion reactions. In addition, these compounds exert a salutary effect in the treatment of symptoms arising from such reactions. They may therefore be employed to diminish the incidence and aid in the symptomatic treatment of nonhemolytic, nonpyrogenic transfusion reactions.

When antihistamines are to be used for prophylactic purposes in protection against symptoms of transfusion reactions, a sterile solution of appropriate concentration may be admixed with the blood at the time of transfusion. This should not be a routine procedure, however, but should be employed only in cases in which there is a known history of nonhemolytic, nonpyrogenic transfusion reations. When appropriate antihistaminic drugs are thus employed, they should be admixed with previously typed and cross matched blood at the time of and not in advance of transfusion. Adequate precautions against contamination should be observed; if a single dose ampul is not available, a previously unopened multiple dose container of the sterile drug solution should be used. For the symptomatic treatment of transfusion reaction, solutions of appropriate concentration may be administered by slow intravenous injection. The oral route should be substituted as soon as possible.

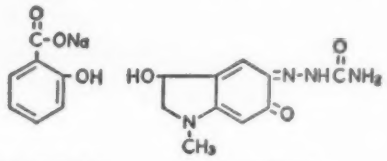
The dosage, which may be repeated every 4 to 6 hours, is the same whether administerd in admixture with blood or as an intravenous injection. For chlorpheniramine maleate, the usual dose is 10 mg.; for diphenhydramine hydrochloride, 50 mg.; for methapyrilene hydrochloride, 20 mg.; and for tripelennamine hydrochloride, 25 mg.

The Council voted to amend New and Nonofficial Remedies accordingly to recognize this additional use of the injectable antihistaminic drugs.

Ciba Pharmaceutical Products, Inc.; Eli Lilly & Company; Parke, Davis & Company; and Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of injectable antihistaminic drugs for the prevention and treatment of blood transfusion reactions.
—*J. Am. Med. Assoc.* *160*:777 (Mar. 3, 1956)

Carbazochrome Salicylate — Adrenosem® Salicylate

CARBAZOCHROME SALICYLATE is Adrenochrome monosemicarbazone sodium salicylate complex.—The structural formulas of sodium salicylate and adrenochrome monosemicarbazone may be represented as follows:



Sodium Salicylate — Adrenochrome Monosemicarbazone

Actions and Uses

Carbazochrome salicylate is a derivative of adrenochrome, an oxidation product of epinephrine, proposed for systemic control of capillary bleeding characterized by increased capillary permeability. The drug does not affect blood pressure, cardiac rate or output, blood clotting mechanism, massive hemorrhage, or arterial bleeding. The use of the drug as a systemic hemostatic is based upon uncontrolled case reports of clinical observers who reported beneficial effects after oral or parenteral administration in controlling the bleeding associated with idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, and hematuria. Carbazochrome salicylate also is claimed to be of value in controlling postpartum hemorrhage and postoperative bleeding associated with tonsillectomy, adenoidectomy, surgery of the nasopharynx, prostate, bladder, chest, and teeth. The drug appears to be relatively nontoxic, and such untoward effects as might arise from repeated use are likely to result from sensitivity to the salicylate component.

'Co-Deltra'

(Prednisone, Buffered)

1956

'Co-Hydeltra'

(Prednisolone, Buffered)

1956

Deltra®

(Prednisone, Merck)

1955

'Hydeltra'

(Prednisolone, Merck)

1955

Alflorone®

Acetate
(Fludrocortisone Acetate, Merck)

1954

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HydroCortone®

(Hydrocortisone, Merck)

1952

Cortone®

Acetate
(Cortisone Acetate, Merck)

1950

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF MERCK & CO., INC.

In the reports of clinical studies so far available there is a lack of adequate controlled clinical evidence to prove that cessation of capillary bleeding can be attributed to the action of this drug. Its clinical usefulness for this purpose is scientifically unestablished.

Dosage

The drug has been administered orally or intramuscularly. The proposed oral dose for adults ranges from 1 to 5 mg. four times daily. The intramuscular dose, which may produce pain during injection, is 5 mg. every 2 to 4 hours. Dosage for children is reduced proportionately.

Preparations for use as stated for the foregoing drug are marketed under the following name: Adrenosem Salicylate.

S. E. Massengill Company cooperated by furnishing scientific data to aid in the evaluation of carbazochrome salicylate.

—*J. Am. Med. Assoc.* *160*:119 (Jan. 14, 1956)

Preparations

Injection Carbazachrome (Adrenosem) Salicylate 5 mg./ml.; 1 ml. ampuls.

Syrup Carbazochrome (Adrenosem) Salicylate 2.5 mg./5 ml.

Tablets Carbazochrome (Adrenosem) Salicylate 1 mg. and 2.5 mg.

Chloramphenicol

Intramuscular Use

The Council has been requested to evaluate the effectiveness of chloramphenicol by the intramuscular route. On the basis of currently available evidence, the Council concluded that the intramuscular administration of this antibiotic is justified in the treatment of typhoid and other serious infections caused by organisms that are susceptible to its action. When chloramphenicol is administered by this route as a microcrystalline suspension, blood levels are maintained for a longer period than for those obtained with equal oral doses. The usual adult dose of an intramuscular suspension is 1 gm. every 8 to 12 hours. In children weighing 15 kg. (33 lb.) or less, 100 to 150 mg. per kilogram of body weight may be injected daily in three or four divided doses.

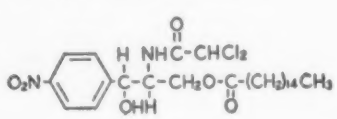
The Council voted to amend New and Nonofficial Remedies accordingly to recognize this additional route of administration of chloramphenicol.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of chloramphenicol.
—*J. Am. Med. Assoc.* *160*:671 (Feb. 25, 1956)

Chloramphenicol Palmitate

Chloromycetin® Palmitate

CHLORAMPHENICOL PALMITATE is D-(-)Threo-1-(*p*-nitrophenyl)-2-dichloroacetamido-1,3-propanediol 3-palmitate.—The structural formula of chloramphenicol palmitate may be represented as follows:



Actions and Uses

Chloramphenicol palmitate represents the esterification of the antibiotic to a tasteless substance for the purpose of circumventing the bitter taste inherent in the parent drug. In the upper intestinal tract, the ester is hydrolyzed back to free chloramphenicol by the action of pancreatic and intestinal lipases. Its chemotherapeutic activity therefore is produced almost solely by release of active chloramphenicol, since the ester itself is practically devoid of antimicrobial action. Absorption of released chloramphenicol is somewhat slower than that of the free antibiotic, but blood levels persist for longer periods of time. The ester may be employd in the treatment of all infections for which the parent drug is indicated. Since chloramphenicol palmitate possesses the same inherent toxicity as the parent drug, the restrictions specified under chloramphenicol apply also to the palmitate; thus, adequate blood studies should be made when prolonged or intermittent administration is required. (See the monograph on chloramphenicol in New and Nonofficial Remedies.)

Dosage

Chloramphenicol palmitate is given orally. Since the dosage is expressed in terms of the parent drug, it is the same as for orally given chloramphenicol.

Preparations for use as stated for the foregoing drug are marketed under the following name: Chloromycetin Palmitate.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of chloramphenicol palmitate.

—*J. Am. Med. Assoc.* *160*:119 (Jan. 4, 1956)

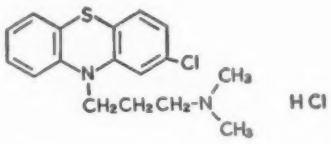
Preparations

Suspension, Oral, Chloramphenicol (Chloromycetin) Palmitate 125 mg./4 ml.; 60 ml. bottles.

Chlorpromazine Hydrochloride

Thorazine® Hydrochloride

CHLORPROMAZINE HYDROCHLORIDE is 2-Chloro-10-(3-dimethylaminopropyl)phenothiazine hydrochloride.—The structural formula of chlorpromazine hydrochloride may be represented as follows:



Actions and Uses

Chlorpromazine hydrochloride, one of the phenothiazine group of compounds, produces depression of the central nervous system. Generally, the electroencephalographic patterns are not altered with the usual dose in normal patients, although some variation has occasionally been reported. It suppresses or abolishes conditioned reflexes in trained rats. It also exhibits a depressant action on certain neural centers in experimental animals, resulting in suppression of vomiting from apomorphine hydrochloride, irradiation, and motion sickness, but, in animals, does not affect the emesis from morphine, veratrum alkaloids, digitalis, and copper sulfate. In addition to these main pharmacological actions, chlorpromazine hydrochloride also possesses

THORAZINE*...*dramatic in emergencies*

vomiting
alcoholism
severe pain
hiccups
acute excitement
status asthmaticus

	Package Size	Price to Hospital
Ampuls 1 cc. 25 mg.	Boxes of 6 Packages of 100 **Packages of 500†**	$3.12 box 44.00 pkg. **195.00 pkg.**
Ampuls 2 cc. 50 mg.	Boxes of 6 Packages of 100 **Packages of 500†**	4.38 box 62.00 pkg. **240.00 pkg.**
Suppositories 25 mg.	Boxes of 6	1.23 box
Suppositories 100 mg.	Boxes of 6	1.53 box
Syrup 10 mg./5 cc.	4 fl. oz. bottles	1.53 each
Tablets 10 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	2.13 each 20.24 each **170.00 each**
Tablets 25 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	3.03 each 28.79 each **243.00 each**
Tablets 50 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	3.63 each 34.20 each **270.00 each**
Tablets 100 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	4.83 each 46.32 each **366.00 each**
Tablets 200 mg.	Bottles of 500 **Bottles of 5000†**	64.85 each **510.00 each**

†Available only to *non-profit* (tax exempt) institutions for use within the institution.

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

weak adrenolytic, hypotensive, antispasmodic, hypothermic, and antihistaminic effects and is capable of potentiating the action of many other agents.

Chlorpromazine hydrochloride is effective when administered orally, intramuscularly, or intravenously. The onset of action is rapid, particularly after parenteral administration. Little is known concerning the metabolic fate of the drug in the body, although current evidence suggests the liver as a possible site of detoxication. After repeated doses, a slight amount of tolerance develops, particularly to the hypotensive and hypnotic effects.

Chlorpromazine hydrochloride has been found useful for the treatment of the nausea and vomiting associated with certain disorders including carcinomatosis, uremia, acute infections, and nitrogen-mustard therapy. Although the use of chlorpromazine hydrochloride in pregnancy for the usual "morning sickness" of the first trimester must be regarded as experimental, it may be tried for controlling hyperemesis gravidarum as a complication of pregnancy, preferably before the onset of liver damage. Its antiemetic effect has been reported as useful in radiation sickness, for the nausea and vomiting produced by certain drugs (including some antibiotics), and for the control of postanesthetic and postoperative nausea and vomiting. It has not been successful in motion sickness. Chlorpromazine hydrochloride often is successful in controlling hiccups refractory to other forms of therapy and in the treatment of status asthmaticus. The drug finds its widest use in alleviating manifestations of anxiety, tension, agitation, and of lessening motor activity in both psychoneurotics and psychotics. The latter include selected cases of schizophrenia, mania, and toxic and senile psychoses. The sedative, tranquilizing, and calming properties of the drug also make it useful as an adjunct in the treatment of certain other mental disorders and in a variety of apparently unrelated conditions where emotional stress is a complicating, or even a causative, factor. It has been used successfully in some depressions where agitation and anxiety are complications. It appears to be of no value in reducing the frequency or intensity of seizures in epilepsy.

The sedative and antiemetic actions of chlorpromazine hydrochloride have been reported to facilitate treatment in acute alcoholism. Its value in narcotic drug withdrawal is not yet established. It has been used in surgical procedures, in obstetrics, and in the treatment of severe pain, especially in cancer patients, for its tranquilizing effects. Its alleged potentiation of hypnotics, sedatives, analgesics, and anesthetics is difficult to evaluate. At the present time, therefore, all these uses should be regarded as unestablished.

Chlorpromazine hydrochloride produces a number of side-effects and toxic reactions, some of which are serious. Cases of severe and fatal blood dyscrasias, including agranulocytosis, in some instances associated with hypoplastic anemia and leukopenia, have been reported after use of this drug. It should be immediately discontinued if patients exhibit evidence of bone marrow depression; physicians should also be alert for any toxic hematopoietic effects, fever, or sore throat. Peripheral blood cell counts are indicated at the onset of such symptoms during therapy.

Jaundice occurs in a significant percentage of patients receiving chlorpromazine. It usually occurs during the first two weeks of treatment but occasionally may not be evident until some time after discontinuance of the drug. There is no correlation between the occurrence of jaundice and dose used, but administration should be promptly halted at the first indication of impending icterus and the appearance of bilirubinuria. Most cases of chlorpromazine-induced jaundice clear within a few weeks after cessation of therapy; however, until longer experience is gained and more knowledge concerning the pathogenesis of this type of jaundice is acquired, physicians are cautioned against administration of the drug to patients with either the presence or history of jaundice or liver damage.

Orthostatic hypotension is a frequent side-effect of chlorpromazine therapy, particularly after parenteral administration. The drug should be given with extreme caution to patients with arteriosclerosis, cardiovascular disease, or other conditions in which a sudden drop in blood pressure may be undesirable. When parenteral administration is to be carried out, the patient must remain in the supine position for at least one hour after the injection. When necessary, pressor agents such as phenylephrine hydrochloride or levarterenol bitartrate may be used to control hypotension. Alarming reactions with failure to respond to pressor agents have been reported from even small intravenous doses. Epinephrine should never be used for this purpose, since the adrenolytic action of chlorpromazine hydrochloride may cause epinephrine reversal.

Sedation and drowsiness, which are desired therapeutic effects in the treatment of acute anxiety and severe agitation, may become unwanted side-effects in other conditions. Other side-effects include tachycardia, hypothermia, dryness of the mouth, dermatitis, photosensitivity, nausea and vomiting, and a Parkinson-like syndrome. With the exception of the latter condition, most side-effects are usually not severe enough to warrant discontinuing the drug therapy. Because of its potentiating action with many other drugs, chlorpromazine hydrochloride should be used with caution in conjunction with other agents, particularly barbiturates, narcotics, and general anesthetics. Its use is contraindicated in comatose patients or those under the influence of large doses of alcohol or other central nervous system depressants.

Chlorpromazine hydrochloride is a potent agent with complex pharmacological actions and important toxic effects and side-reactions. Although its therapeutic range of effectiveness is wide, sufficient experience has not been gained to determine its ultimate place in the therapeutic armamentarium. Physicians accordingly should weigh the beneficial effects to be gained against the possible toxic reactions and side-effects.

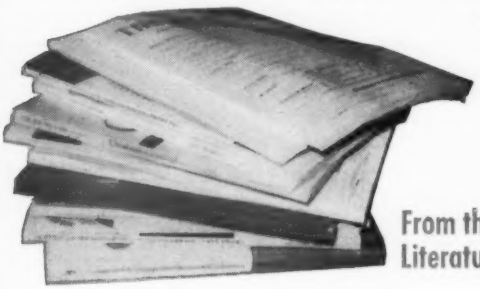
Dosage

Chlorpromazine hydrochloride is administered orally, intramuscularly, or intravenously. The dosage must be highly individualized from patient to patient according to the severity of the condition and the degree of response; the smallest effective dose should always be used. Oral dosage ranges from 10 to 400 mg. or more per day. Dosage for children is reduced proportionately. Deep intramuscular injection is the preferred parenteral route, with the dosage for adults ranging from 25 mg. per day for mild nausea and vomiting to as much as 400 mg. per day for acutely agitated manic patients. Because of the added danger of severe hypotension, extreme caution should be exercised in giving the drug intravenously. Because of reported instances of fatal shock, all forms of parenteral administration should usually be reserved for bedfast or hospitalized patients.

Preparations for use as stated for the foregoing drug are marketed under the following name: Thorazine Hydrochloride.

PARENZYME® INTRAMUSCULAR TRYPSIN

in HOSPITAL USE



From the Literature

"It is difficult to fail to be impressed with a drug which like penicillin, or cortisone, has an almost accurately predictable and unfailing effect, and which is capable of revising pathological changes of long standing."[1]

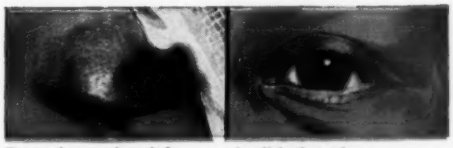
"It (intramuscular trypsin) is effective in extraocular trauma, uveal tract inflammation, in anterior and in some posterior chamber hemorrhages of recent origin."[2]

"A salutary effect on the thrombophlebitic process was elicited. The per patient hospital stay averaged 19 plus days for those not receiving trypsin, against 9 plus for those who did receive it."[3]

Direct anti-edema, anti-inflammatory action has many applications in the wards, emergency rooms and outpatient clinics.

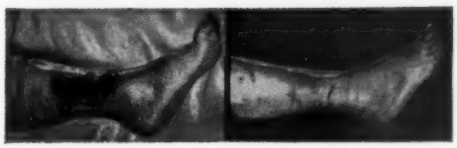
Advantages of PARENZYME, *Intramuscular Trypsin:*

- Safe method of administering parenteral trypsin; no major side effects; not anticoagulant
- can be used in conjunction with any other therapy prescribed
- early ambulation and return to full activity
- no metabolic derangements such as often occur with other anti-inflammatory agents
- known amount of active enzyme is used
- tends to enhance use of antibiotic therapy



Deep laceration left eyebrow. Penicillin administered, condition worsened, marked edema, pre-auricular adenopathy, pain.

Antibiotics plus Parenzyme administered. 24 hours improvement. 48 hours eye opened. Rapidly healing.



Female diabetic, 72 years old. Peripheral arteritis obliterans, with cellulitis and gangrenous ulcerations. Burning pain.

Parenzyme administered daily. Healing of ulcer complete. Pain and edema eliminated.

Time between photos 9 weeks.

INDICATIONS: The cardinal indication for Parenzyme is acute inflammation regardless of etiology.

TRAUMATIC WOUNDS: slow-healing wounds, bruises, contusions, black eyes.

SKIN ULCERS: decubitus, varicose, diabetic.

VASCULAR DISORDERS: phlebitis, thrombophlebitis, phlebothrombosis.

OPHTHALMIC: iritis, iridocyclitis, chorioretinitis.

The film, CLINICAL ENZYMOLOGY, is available for showing at all hospital meetings upon request.

DOSAGE: 2.5 mg. (0.5 ml.) intragluteally q. 6 h. until improvement results; q. 12 h. thereafter. RECOMMENDED METHOD OF INJECTION: Very slowly intragluteally.

SUPPLIED: 5 ml. multiple-dose vials (5 mg. trypsin/ml.)

REFERENCES: 1. Wildman, P. J. Intramuscular Trypsin in the Treatment of Chronic Thrombophlebitis, Angiology, Oct. 1955. 2. Campagna, F. N. and Hopen, J. M., Trypsin in Ocular Disease. Delaware State Medical Journal, 27, March 1955. 3. Seligman, B. Clinical Experience with Trypsin, Ohio State Medical Journal, 51, May 1955.

PRODUCTS OF ORIGINAL RESEARCH

NATIONAL NATIONAL NATIONAL NATIONAL NATIONAL NATIONAL

THE NATIONAL DRUG COMPANY

Smith, Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of chlorpromazine hydrochloride.
—*J. Am. Med. Assoc.* *160*:287 (Jan. 28, 1956)

Preparations

Injection Chlorpromazine (Thorazine) Hydrochloride 25 mg./ml.; 1 ml. and 2 ml. ampuls.

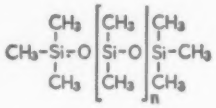
Suppositories Chlorpromazine (Thorazine) 25 mg. and 100 mg.

Syrup Chlorpromazine (Thorazine) Hydrochloride 10 mg./4 ml.; 120 ml. bottles.

Tablets Chlorpromazine (Thorazine) Hydrochloride 10 mg., 25 mg., 50 mg., 100 mg., and 200 mg.

Dimethicone — Silicote®

DIMETHICONE is a silicone oil consisting of dimethylsiloxane polymers and technically designated as dimethylpolysiloxane of the D. C. 200 series of fluids. The structural formula of dimethicone may be represented as follows:



Actions and Uses

Dimethicone, a silicone oil with skin-adherent and water-repellent properties, is useful for incorporation into ointment bases as a skin protective agent. Either greasy or relatively nongreasy preparations may be suitable, depending upon the conditions of exposure for which protection is desired. Greasy bases generally are better tolerated on skin that is excessively dry or that may be exposed to drying effects, but they may not be feasible in some industries. Relatively greaseless bases are subject to the disadvantage of easier removal and thus may provide less continuous protection. When applied to the skin in such vehicles, dimethicone imparts a coating effect that generally is resistant for a variable period of time to ordinary soap and water and to water-soluble irritants. Its resistance to nonsoap detergents and oil-miscible substances is less certain and there is some difference of opinion regarding its ability to repel organic solvents and different types of industrial oils. These differences appear to be influenced by the type of vehicle, although the comparative length of time for which protection is afforded by various preparations has not been determined. There is also lack of evidence to demonstrate that a given preparation of dimethicone offers better protection than use of the base alone. The addition of dimethicone, however, is regarded as an advance in the field of skin protective preparations.

Dimethicone is relatively inert and exerts no therapeutic action. It therefore is considered useful for topical application only as a prophylactic against exposure to dermal irritants and to ordinary cleansers and water when these are irritating or interfere with the healing of dermal lesions. Its use has been less successful in preventing dermal contact with household detergents and fuels than with soap and water. The effectiveness of dimethicone also is limited in preventing water or soap from aggravating lesions of chronic dermatoses, such as eczema. Except in chronic dermatoses aggravated by substances that can be repelled by dimethicone, it should be restricted generally to application on the normal skin. The agent may be irritating to the skin of infants and thus is of questionable utility for the prevention of ammoniacal dermatitis (diaper rash). Because of its semiocclusive nature, dimethicone also may be harmful when applied to an acute dermatitis, or otherwise inflamed, traumatized, abraded, or excoriated skin. Likewise, it should not be applied over lesions that require free drainage, such as infected decubitus ulcers, fissures, fistulas, and sinuses. It can be used to prevent maceration and irritation of the skin surrounding such lesions as well as ileostomies and other operative stoma associated with irritating discharges; however, it is not considered helpful in controlling anogenital pruritus, which is seldom caused by associated discharges and may be aggravated by ointment preparations.

Dimethicone does not appear to sensitize the normal skin, but physicians should be alert to the possibility of sensitization from components of the ointment vehicle with which it is incorporated. As used in a base of white petrolatum, three or four surgical-type scrubbings may be required for its removal. Industrial workers should be warned against using solvents to hasten removal, as such agents also may give rise to occupational dermatoses. Dimethicone should not be used in the eyes because it produces a temporary smarting.

Dosage

Dimethicone is applied to the skin in various types of ointment bases. A 30% concentration is used in white petrolatum; other concentrations may be better suited for other types of bases. The area to be protected should first be thoroughly cleansed with soap or a suitable substitute and water. The smallest amount necessary to cover the area should be applied uniformly and rubbed in thoroughly. Initially, application is made three to four times daily for one or two days, then one or two times daily depending upon the nature and frequency of exposure. With a greasy type base, any stickiness that remains after application can be minimized by wiping with a dry cloth or washing gently with soap and water, without removing the protective film. With relatively greaseless bases, care must be exercised to avoid removal during exposure, and more frequent daily applications may be required to provide protection.

Preparations for use as stated for the foregoing drug are marketed under the following name: Silicote.

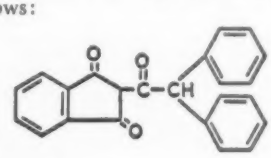
Arnar-Stone Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of dimethicone.
—*J. Am. Med. Assoc.* *160*:118 (Jan. 14, 1956)

Preparations

Ointment Dimethicone (Silicote).

Diphenadione — Dipaxin®

DIPHENADIONE is 2-Diphenylacetyl-1,3-indandione.—The structural formula of diphenadione may be represented as follows:



Actions and Uses

Diphenadione is an orally effective synthetic anticoagulant closely related chemically to another indandione derivative, phenindione, and also qualitatively similar in action and uses to coumarin derivatives

for diarrhea..

LACTINEX®

Granules & Tablets

LACTINEX GRANULES and LACTINEX TABLETS contain a standardized viable mixed culture of Lactobacilli acidophilus and bulgaricus with the naturally-occurring metabolic enzymes produced by these organisms.

LACTINEX TABLETS—A clinically proven treatment for gastrointestinal disturbances, including diarrhea[1,2] (antibiotic induced and others) in infants and adults.

LACTINEX GRANULES—An especially designed dosage form (served on cereal, food or with milk) of this effective product for the pediatric and geriatric patient.

Dosage: Three or four tablets or one packet, three or four times a day.

Supplied—tablets in bottles of fifty—granules in boxes of twelve, one gram packets.

1. *Siver, Robert H.: Current Medical Digest, Vol. XXI, No. 9, September 1954.*
2. *McGivney, John: Texas State Journal of Medicine, Vol. 51, No. 1, January 1955.*

HWD

HYNSON, WESTCOTT & DUNNING, INC., Baltimore I, Md.

such as bishydroxycoumarin. Like these agents, it inhibits blood coagulation by reducing the concentration of prothrombin and related factors; this is useful in the prevention and treatment of conditions characterized or complicated by intravascular clotting, but does not directly affect thrombi or emboli already formed or increase the blood supply to infarcted areas.

Since diphenadione is one of the most potent and prolonged-acting depressants of blood prothrombin activity, it is effective in smaller doses than most other oral anticoagulants. Adequate depression of blood prothrombin levels (prolongation of prothrombin time) usually is obtained within 48 to 72 hours after administration of the initial recommended dosage. This depression may persist for as long as 20 days after cessation of maintenance therapy.

Diphenadione has approximately the same ratio between its effective and toxic (hemorrhagic) dosage as other oral anticoagulants, so that similar care is necessary to avoid overdosage and hemorrhagic complications. Prothrombin time determinations should be made prior to treatment and daily until the effective maintenance dosage is established. Thereafter, prothrombin determinations at weekly or not longer than 10-day intervals may be sufficient. For most purposes, the prothrombin time should be prolonged from two to two and one-half times a standard normal time of 15 seconds. Undue hypoprothrombinemia and hemorrhagic complications not controlled by withdrawal of medication may be counteracted by phytonadione (vitamin K_1) and, when necessary, transfusion of whole blood.

So far, diphenadione has not been observed to produce untoward effects; however, because of its chemical similarity to phenindione, which has been reported to produce agranulocytosis, physicians should obtain periodic blood cell counts during prolonged therapy until sufficient experience has been gained to determine its long-term effects on the blood.

Dosage

Diphenadione is administered orally. The suggested initial dosage, after determination of a normal prothrombin time, is 20 to 30 mg. the first day and 10 to 15 mg. the second day. When a prompt anticoagulant effect is indicated, initial medication can be supplemented by the concomitant intravenous administration of heparin sodium to achieve the desired prothrombin suppression. If the prothrombin time is more than 30 seconds at the end of the second day (48 hours), further therapy should be withheld until the prothrombin time starts to decrease. Thereafter the suggested daily doses of diphenadione are adjusted as follows: with a prothrombin time between 20 and 30 seconds, a dose of 10 to 15 mg.; with a prothrombin time between 30 and 35 seconds, a dose of 7 to 10 mg; with a prothrombin time between 35 and 40 seconds, a dose of 5 mg. If the prothrombin time increases rapidly to more than 40 seconds during induction of therapy, or if there is a rapid increase during maintenance therapy, the dose should be withheld or only a small dose (1 to 2 mg.) administered on that day. The average daily maintenance dose is usually 3 to 5 mg. and should be adjusted to maintain prothrombin time between 30 to 37 seconds. Patients should be instructed to report any evidence of bleeding and to discontinue further medication immediately if the physician cannot be reached.

Preparations for use as stated for the foregoing drug are marketed under the following name: Dipaxin.

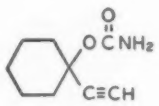
The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of diphenadione.
—*J. Am. Med. Assoc.* 160:776 (Mar. 3, 1956)

Preparations

Tablets Diphenadione (Dipaxin) 5 mg., scored.

Ethinamate — Valmid®

ETHINAMATE is 1-Ethynylcyclohexyl carbamate. The structural formula of ethinamate may be represented as follows:



Actions and Uses

Ethinamate is related chemically to the carbamate series of compounds, which exert only a feeble depressant effect, but it contains an ethinyl group that contributes to this action. It does not produce antipyretic, analgesic, or diuretic action, but it does exhibit a mild sedative effect on the central nervous system. Its duration of action is shorter than that produced by the barbiturate somnifacients. Ethinamate thus is useful chiefly as a hypnotic for the prompt induction of sleep in simple insomnia. When a single initial (bedtime) dose is effective for this purpose, the shorter action of the drug produces little or no hypnotic after-effect such as is occasionally observed with hypnotic doses of barbiturates; however, this possible advantage is likely to be lost in severe insomnia, when repeated doses of ethinamate are required to insure sleep throughout the night. For this reason, the drug is not primarily suited for use in patients requiring heavy or continuous sedation. The drug can be tried as a daytime sedative, however, for patients sensitive to barbiturates.

Ethinamate is readily absorbed by the gastrointestinal tract, and the major portion of the drug is rapidly destroyed in the body. About one-tenth to one-third of the oral dose is excreted in the urine. The liver is not the principal site of destruction of the drug in the body.

Ethinamate has not been found to produce toxic effects in man or experimental animals. Tachyphylaxis, tolerance, euphoria, and physical dependence have not been observed. The drug may be employd in the presence of impaired liver or kidney function, but until longer experience is gained, particularly with the prolonged use of the larger doses that may be required for effective hypnosis or continuous sedation, physicians should be alert for the occurrence of any unusual toxic effects.

Dosage

Ethinamate is administered orally. The minimal effective hypnotic dose for adults is 0.5 gm. taken 20 minutes before retiring. Some patients may require as much as 2 gm. to induce sleep or a further dose on awakening before morning.

Preparations for use as stated for the foregoing drug are marketed under the following name: Valmid.

Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of ethinamate.
—*J. Am. Med. Assoc.* 160:289 (Jan. 28, 1956)

Preparations

Tablets Ethinamate (Valmid) 0.5 Gm., scored.

hospitals can't afford part-time diuretics

Maximum therapeutic benefit with minimal side effects—rapidly achieved—are the criteria for drugs most valued in hospital practice.

That is why more hospitals choose MERCUHYDRIN as the injectable which almost invariably gives more rapid relief of heart failure. Once patient's acute symptoms are controlled, NEOHYDRIN, the most effective oral diuretic, maintains their improvement. It continues steady diuresis, requires no rest periods and rarely requires discontinuance because of side effects.

for full-time, every-time diuresis

by injection **MERCUHYDRIN®** sodium
(BRAND OF MERALLURIDE INJECTION)

TABLET

by mouth **NEOHYDRIN®**
(BRAND OF CHLORMERODRIN)

LAKESIDE

Hydrocortisone

Intramuscular Use

The Council has been requested to evaluate the intramuscular use of hydrocortisone (free alcohol). On the basis of currently available evidence, the Council concluded that the intramuscular injection of this hormone is justified as a temporary substitute for oral medication or as a supplement to intravenous administration in emergency situations amenable to intense gluco-steroid therapy. The free alcohol is more rapidly absorbed and therefore more promptly effective than hydrocortisone acetate. The usual daily dose of hydrocortisone by the intramuscular route is the same as that by the oral route.

The Council voted to amend New and Nonofficial Remedies accordingly to recognize this additional route of administration of hydrocortisone.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of the intramuscular use of hydrocortisone.

—*J. Am. Med. Assoc. 160*:777 (Mar. 3, 1956)

Hydrocortisone Acetate

In the Treatment of Ganglion

The Council has recognized the proposed additional use of hydrocortisone acetate for treatment of aponeurotic or tendon cysts (ganglions). For this purpose, 0.3 to 0.5 cc. of a suspension of the drug containing 25 mg. per cubic centimeter is injected directly into the cyst cavity. The Council concluded that the procedure was reasonable for and beneficial in some cases of ganglion to promote resolution of the process but that longer follow-up experience was required to determine the permanence of its variable eradicative effect and its comparison with other methods of treatment.

The Council voted to expand the New and Nonofficial Remedies monograph on hydrocortisone acetate accordingly.

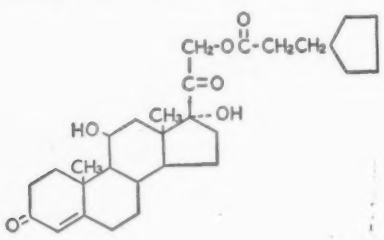
Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of hydrocortisone acetate.

—*J. Am. Med. Assoc. 160*:51 (Jan. 7, 1956)

Hydrocortisone Cyclopentylpropionate

Cortef® Fluid

HYDROCORTISONE CYCLOPENTYLPROPIONATE is 17-Hydroxycorticosterone-21-cyclopentylpropionate. The structural formula of hydrocortisone cyclopentylpropionate may be represented as follows.



Actions and Uses

Hydrocortisone cyclopentylpropionate, an ester of hydrocortisone, exhibits the same systemic actions and has the same potency as equivalent amounts of hydrocortisone. It is somewhat more palatable and more slowly absorbed from the gastrointestinal tract than the parent hormone. (See the monograph on hydrocortisone in New and Nonofficial Remedies.)

Dosage

Hydrocortisone cyclopentylpropionate is administered orally. The dosage, expressed in terms of the parent drug, is the same as for hydrocortisone. (See the monograph on hydrocortisone in New and Nonofficial Remedies.)

Preparations for use as stated for the foregoing drug are marketed under the following name: Cortef Fluid.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of hydrocortisone cyclopentylpropionate.

—*J. Am. Med. Assoc. 160*:289 (Jan. 28, 1956)

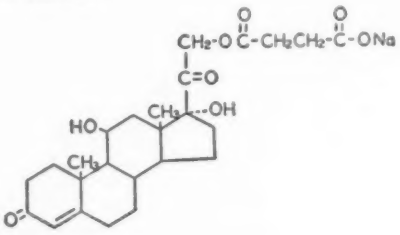
Preparations

Suspension, Oral, Hydrocortisone (Cortef Fluid) Cyclopentylpropionate 10 mg./5 ml.; 120 ml. bottles.

Hydrocortisone Sodium Succinate

Solu-Cortef®

HYDROCORTISONE SODIUM SUCCINATE is Sodium 17-hydroxycorticosterone-21-succinate. The structural formula of hydrocortisone sodium succinate may be represented as follows:



Actions and Uses

Hydrocortisone sodium succinate is a highly soluble ester-salt of hydrocortisone with the same actions as the parent hormone. In general, the indications for its use are the same as for an infusion concentrate solution of hydrocortisone, but its greater solubility makes possible its administration in much smaller volumes of diluent. Thus, hydrocortisone sodium succinate is suitable for parenteral administration in the management of emergencies amenable to intense corticoid therapy. Its use is indicated in shock-like syndromes resulting from acute adrenal cortical insufficiency, acute hypersensitivity reactions, status asthmaticus, and disseminated lupus erythematosus in relapse and in overwhelming infections with acute toxic reactions in which sufficient time has not elapsed to allow concurrently administered antibiotics to become effective. Since administration of hydrocortisone sodium succinate involves the same inherent dangers as does the use of cortisone or hydrocortisone, its parenteral administration is intended only for short-term emergency therapy (See the general statement on gluco-corticoids in New and Nonofficial Remedies.)

Dosage

Hydrocortisone sodium succinate may be administered intravenously or intramuscularly. The dosage, expressed in terms of the parent drug, is the same as that for hydrocortisone. In emergency situations, a solution containing the equivalent of 100 mg. of hydrocortisone may be dissolved in 2 cc. of sterile water or isotonic sodium chloride solution and administered intravenously over a period of at least one-half minute. Thereafter 50 mg. doses may be similarly injected as required. When it is necessary to continue emergency treatment, intravenous

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Kaopectate

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Each fluidounce contains:
Kaolin . . . . . 90 grs.
Pectin . . . . . 2 grs.
in an aromatized and carminative vehicle
Available in bottles of 6 and 10 fluidounces and 1 gallon

The Upjohn Company, Kalamazoo, Michigan

medication may be replaced by intramuscular injection of 50 mg. doses. These may be repeated at appropriate intervals not to exceed 6 hours during the first day of therapy. In patients with acute hypersensitivity reactions, 100 mg. may be given intravenously every 4 to 6 hours. Hydrocortisone sodium succinate may also be dissolved in sterile isotonic sodium chloride solution containing 5% glucose and administered by intravenous drip. When prolonged gluco-corticoid therapy is indicated, oral medication with cortisone or hydrocortisone should be substituted as soon as practical. (See the monographs on cortisone and hydrocortisone in New and Nonofficial Remedies.)

Preparations for use as stated for the foregoing drug are marketed under the following name: Solu-Cortef.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of hydrocortisone sodium succinate.

—*J. Am. Med. Assoc.* 160:389 (Feb. 4, 1956)

Preparations

Injection Hydrocortisone (Solu-Cortef) Sodium Succinate 100 mg., dry; 10 ml. vials.

Isoproterenol

As an Adjunct in the Treatment of Chronic Pulmonary Emphysema

A review of available evidence and the opinions of clinical consultants indicates that the oral inhalation of a 1:200 solution of isoproterenol (isopropylarterenol) hydrochloride is useful as an adjunct in symptomatic treatment of chronic pulmonary emphysema to relieve bronchospasm, shrink swollen mucous membranes, and reduce the secretion of mucus. The drug previously has been recognized only for controlling attacks of uncomplicated bronchial asthma (New and Nonofficial Remedies 1955, pp. 225-226). It was agreed that the drug cannot be expected to alter the natural course of chronic pulmonary emphysema and that inhalation of the drug may be accompanied by the same undesirable side-effects and is subject to the same precautions as when it is employed for bronchial asthma alone, particularly in patients who recently have received ephedrine or epinephrine. The Council concluded that, since solutions of either the hydrochloride or sulfate salts are suitable for inhalation in the management of bronchial asthma, either can be employed also to clear the airway in chronic pulmonary emphysema.

The Council voted to expand the New and Nonofficial Remedies monographs on isoproterenol hydrochloride and isoproterenol sulfate accordingly.

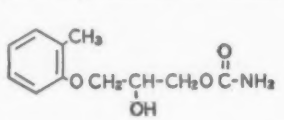
Winthrop Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of isoproterenol hydrochloride.

—*J. Am. Med. Assoc.* 160:50 (Jan. 7, 1956)

Mephenesin Carbamate

Tolseram® Carbamate

MEPHENESIN CARBAMATE is 2-Hydroxy-3-*o*-tolyoxypropyl carbamate. The structural formula of mephenesin carbamate may be represented as follows:



Actions and Uses

Mephenesin carbamate, a salt of mephenesin, exhibits the same systemic actions and has the same uses as the parent drug. (See the monograph on mephenesin in New and Nonofficial Remedies.) Mephenesin carbamate is less soluble than mephenesin and therefore more slowly absorbed from the gastrointestinal tract. Although its duration of action is somewhat longer, the carbamate is not more potent than the parent drug in equivalent amounts.

Dosage

Mephenesin carbamate is administered orally The usual dose for adults is 1 to 3 gm. given three to five times a day, particularly after meals or with milk or fruit juice. Dosage for children should be reduced proportionately.

Preparations for use as stated for the foregoing drug are marketed under the following name: Tolseram.

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of mephenesin carbamate.

—*J. Am. Med. Assoc.* 160:289 (Jan. 28, 1956)

Preparations

Suspension, Oral, Mephenesin (Tolseram) Carbamate 1 Gm./5 ml.

Tablets Mephenesin (Tolseram) Carbamate 0.5 Gm., scored.

Nystatin

Mycostatin®

NYSTATIN is an antibiotic substance isolated from cultures of *Streptomyces noursei*. The chemical identity of nystatin has not been determined.

Actions and Uses

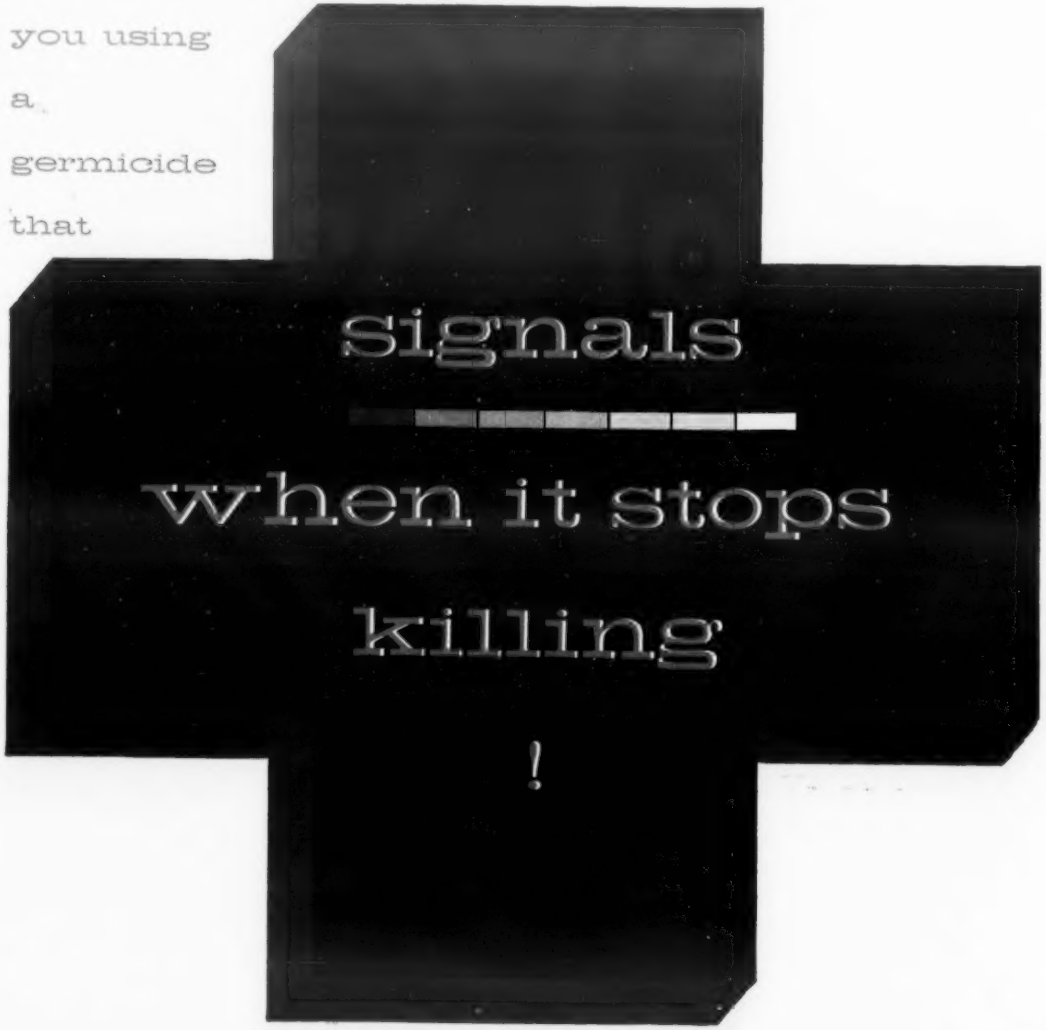
Nystatin is used to treat infections caused by the monilial organism *Candida albicans*. Although the drug is effective in vitro against many yeasts and molds, its clinical usefulness in mycotic infections other than those caused by *Candida* has not been established. Nystatin is poorly absorbed from the gastrointestinal tract and is excreted almost entirely in the feces after oral administration. There is no evidence that the drug is absorbed through the skin or mucous membranes after topical application.

Nystatin has been employed with varying degrees of success in the treatment of all forms of moniliasis, but its ultimate usefulness in controlling various sites of involvement remains undetermined. The drug has been found useful for the topical treatment of moniliasis of the mouth and buccal mucosa (thrush) and for monilial paronychia and other types of cutaneous monilial lesions. Local application of the drug has also been useful in cases of monilial infections of the vagina and labia. Oral administration of nystatin is considered suitable for the treatment of intestinal moniliasis, but the effectiveness of its oral use as an adjunct to local therapy of the skin or mucous membranes is not yet established.

Nystatin has been employed orally for the prophylactic suppression of intestinal fungi and yeasts, particularly *C. albicans*, in patients undergoing oral therapy with broad-spectrum antibiotics. Although the percentage is low, clinical anal or rectal moniliasis develops in some patients in the course of such therapy, presumably because of overgrowth of nonsusceptible monilial organisms. In such patients, the concomitant administration of nystatin and a broad-spectrum antibiotic is indicated.

Oral administration of nystatin has also been proposed for the treatment of systemic moniliasis. Although

are
you using
a
germicide
that



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NONSELECTIVE KILL Exceptionally wide range effectiveness against: bacteria, viruses, fungi, yeasts and other pathogens.

TRIPLES KILL CAPACITY Germicidal capacity is three to four times that of other germicides as tested on successive kills of seven common organisms.

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COSTS LESS It's inexpensive because so little does so much. The usual recommended dilution of 3 oz. to 5 gallons of water (75 ppm available iodine) costs less than 2¢ per gallon.

WESCODYNE is recommended for almost any disinfecting procedure or hospital housekeeping. Unaffected by hard or cold water. Leaves no "hospital smell." Write for full report containing toxicological and microbiological data.

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WEST DISINFECTING Company

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some of the clinical results indicate a transient remission of symptoms, it is difficult to attribute this to an orally administered agent that is poorly absorbed from the gastrointestinal tract. Because of questionable absorption and local irritation, the parenteral use of nystatin is not feasible at present. If, however, an effective method of administration that would provide contact between the systemic pathogens and the agent can be developed, nystatin offers some promise for the treatment of generalized monilial infections. The use of nystatin should be considered established only for it local action in the intestine, on the skin, and on mucous membranes. Nystatin is relatively nontoxic and has few side-effects. The infrequent untoward reactions reported have been mild and transitory, consisting chiefly of nausea, vomiting, and diarrhea after oral administration. Changes in the peripheral blood or blood-forming organs have not been reported after prolonged oral therapy.

Dosage

The dosage of nystatin is expressed in terms of units. For gastrointestinal monilial infection, the proposed dose for adults is 500,000 to 1,000,000 units three times a day. In chronic or resistant anal or vaginal moniliasis, the oral administration of 500,000 units three times daily has been used adjunctively with topical application to overcome or decrease the possibility of reinfection from the intestine. Suspensions of nystatin in water, honey, or other vehicles, containing 100,000 units per cubic centimeter, may be dropped into the mouth or applied locally with a swab to monilial lesions of the mouth. Vaginal infections are treated by the local use, once or twice daily, of suppositories or tablets containing 100,000 units. For cutaneous or mucocutaneous moniliasis, an ointment containing 100,000 units per gram should be applied directly to the mycotic lesions once to several times daily.

If the drug is to be tried for treatment of systemic infections, the proposed oral dose is 1,000,000 units four times daily, and it may be increased beyond this level if side-effects do not become troublesome. The recommended oral dosage for children is 100,000 units three to four times daily.

Preparations for use as stated for the foregoing drug are marketed under the following name: Mycostatin.

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of nystatin.

—*J. Am. Med. Assoc.* *160*:776 (Mar. 3, 1956)

Preparations

Ointment Nystatin (Mycostatin) 100,000 U./Gm.; 30 Gm. tubes.

Suspension, Oral, Nystatin (Mycostatin) 100,000 U./ml., dry; 24 dose bottles.

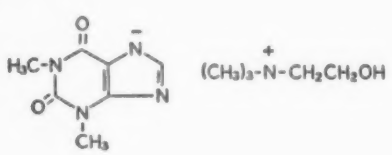
Tablets Nystatin (Mycostatin) 500,000 U.

Tablets, Vaginal, Nystatin (Mycostatin) 100,000 U.

Oxtriphylline

Choledyl®

OXTRIPHYLLINE is Choline theophyllinate.—The structural formula of oxtriphylline may be represented as follows:



Actions and Uses

Oxtriphylline is a theophylline compound that produces the mild diuretic, myocardial stimulating, vasodilator, and bronchodilator actions of similar xanthine derivatives. (See the general statement on xanthine derivatives in New and Nonofficial Remedies.) Oxtriphylline is more soluble than aminophylline; it also appears to be more stable, is better absorbed from the gastrointestinal tract, and produces less gastric irritation. Thus it is tolerated orally in larger doses and produces higher theophylline blood levels than can be achieved with equal doses of aminophylline. Hence, in contrast to theophylline and theophylline compounds, which are poorly tolerated by the stomach, oxtriphylline can be administered orally in doses adequate for the management of bronchial asthma (including pulmonary emphysema) and for the control of paroxysmal cardiac dyspnea and Cheyne-Stokes respiration. Like other theophylline compounds, it is also effective as a mild diuretic for the management of dependent and chronic pulmonary edema secondary to congestive heart failure. The drug also may be tried in selected cases of angina pectoris and coronary disease whenever myocardial stimulation would not be harmful. Its usefulness in premenstrual tension or in dysmenorrhea has not been established.

Oxtriphylline is essentially nontoxic at clinically effective dosage levels. Comparative studies with other theophylline compounds that are well tolerated orally have not been made.

Dosage

Oxtriphylline is administered orally. In the treatment of asthma, dosage for adults may range from 0.1 to 0.4 gm., four times daily. The recommended initial dosage is 0.2 gm. Two weeks or more may elapse before the full effect develops. The usual dosage for children 6 years of age or older is 0.1 gm. three or four times daily; the drug is not recommended for younger children.

Preparations for use as stated for the foregoing drug are marketed under the following name: Choledyl.

Nepera Chemical Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of oxtriphylline.

—*J. Am. Med. Assoc.* *160*:467 (Feb. 11, 1956)

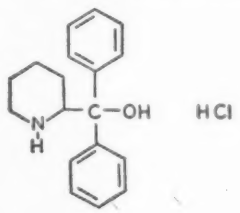
Preparations

Tablets Oxtriphylline (Choledyl) 100 mg. and 200 mg.

Pipradrol Hydrochloride

Meratran® Hydrochloride

PIPRADROL HYDROCHLORIDE is *a,a*,-Diphenyl-2-piperidinemethanol hydrochloride.—*a*-(2-Piperidyl) benzhydrol hydrochloride.—The structural formula of pipradrol hydrochloride may be represented as follows:



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Promazine Hydrochloride

10-[3-dimethylamino-n-propyl]-phenothiazine hydrochloride

For the Management of the Acutely Agitated Patient

• ***The acute alcoholic*** • ***The acute psychotic*** • ***The drug addict***

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Supplied: Tablets, 25, 50, and 100 mg., bottles of 50 and 500; 200 mg., bottles of 500. Injection, 50 mg. per cc., vials of 2 and 10 cc.

1. Seifter, J., et al.: To be published. 2. Fazekas, J.F., et al.: M. Ann. District of Columbia **25**:67 (Feb.) 1956. 3. Mitchell, E.H.: J.A.M.A. In press.

*Trademark

Wyeth

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An Exclusive Development of Wyeth Research

Actions and Uses

Pipradrol hydrochloride is a central nervous system stimulant chemically unrelated to the sympathomimetic amines but exhibiting some of the pharmacological actions of amphetamine. The drug induces supramedullary stimulation from doses that are much smaller than those required to produce death; disorganized motor activity or convulsions are noted only when the dosage approaches lethal levels. Pipradrol hydrochloride produces less anorexia, insomnia, and euphoria than does amphetamine and in therapeutic doses has little effect on heart rate, blood pressure, or respiration. It is absorbed rapidly from the gastrointestinal tract, but its action is somewhat irregular and of short duration. Cumulative effects have not been noted.

Pipradrol hydrochloride has been used as a cortical stimulant in depressive states that are not associated with strong anxiety or compulsive behavior. It has been reported useful in relieving emotional and mental depression objectively but often not subjectively and in producing an elevation in mood depressions often encountered in old age and chronic disease. Although the drug has been studied sufficiently to warrant its trial in these conditions, its ultimate place in the therapeutic armamentarium remains to be determined by subsequent investigation and experience. It is not recommended at this time for frank psychoses or adjunctively in organic systemic diseases for which the drug has not been adequately evaluated clinically.

At present pipradrol hydrochloride seems to have a wide margin of safety and appears to be relatively nontoxic, even when doses in excess of the recommended therapeutic level are administered. Such side-effects as have been reported may be attributed to its central stimulant action and include mild hyperexcitability, anorexia, and insomnia. Though these are generally mild, the patient should be informed of their possible occurrence. The drug is contraindicated in agitated, prepsychotic patients, paranoia, and in cases in which hyperexcitability, anxiety, chorea, or obsessive-compulsive states are present.

Dosage

Pipradrol hydrochloride is administered orally. The recommended dose for adults is 1 to 2 mg. three times a day. The individual response to the drug is somewhat variable; unless patients are carefully selected, some will fail to exhibit any kind of favorable response after fairly high doses. The drug is not recommended for children at the present time.

Preparations for use as stated for the foregoing drug are marketed under the following name: Meratran Hydrochloride.

The Wm. S. Merrell Company cooperated by furnishing scientific data to aid in the evaluation of pipradrol hydrochloride.

—*J. Am. Med. Assoc.* *160*:390 (Feb. 4, 1956)

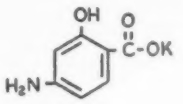
Preparations

Tablets Pipradrol (Meratran) Hydrochloride 1 mg. and 2.5 mg.

Potassium Aminosalicylate

Paskalium®
Paskate®

POTASSIUM AMINOSALICYLATE is the potassium salt of aminosalicylic acid.—The structural formula of potassium aminosalicylate may be represented as follows:



Actions and Uses

Potassium aminosalicylate shares the action and use of the parent drug, aminosalicylic acid, and its other salts in the chemotherapy of tuberculosis. (See the monograph on aminosalicylic acid in New and Nonofficial Remedies.) There is some evidence that the potassium salt may cause less gastric intolerance than the acid or sodium salt. It can be used in place of the sodium salt for patients required to restrict their sodium intake, but otherwise is subject to the same precautions and side-effects.

Dosage

Potassium aminosalicylate is administered orally. The average dosage for adults is 12 gm. daily in three or four divided doses.

Preparations for use as stated for the foregoing drug are marketed under the following names: Paskalium; Paskate.

Glenwood Laboratories, Inc. and Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of potassium aminosalicylate.

—*J. Am. Med. Assoc.* *160*:1143 (Mar. 31, 1956)

Preparations

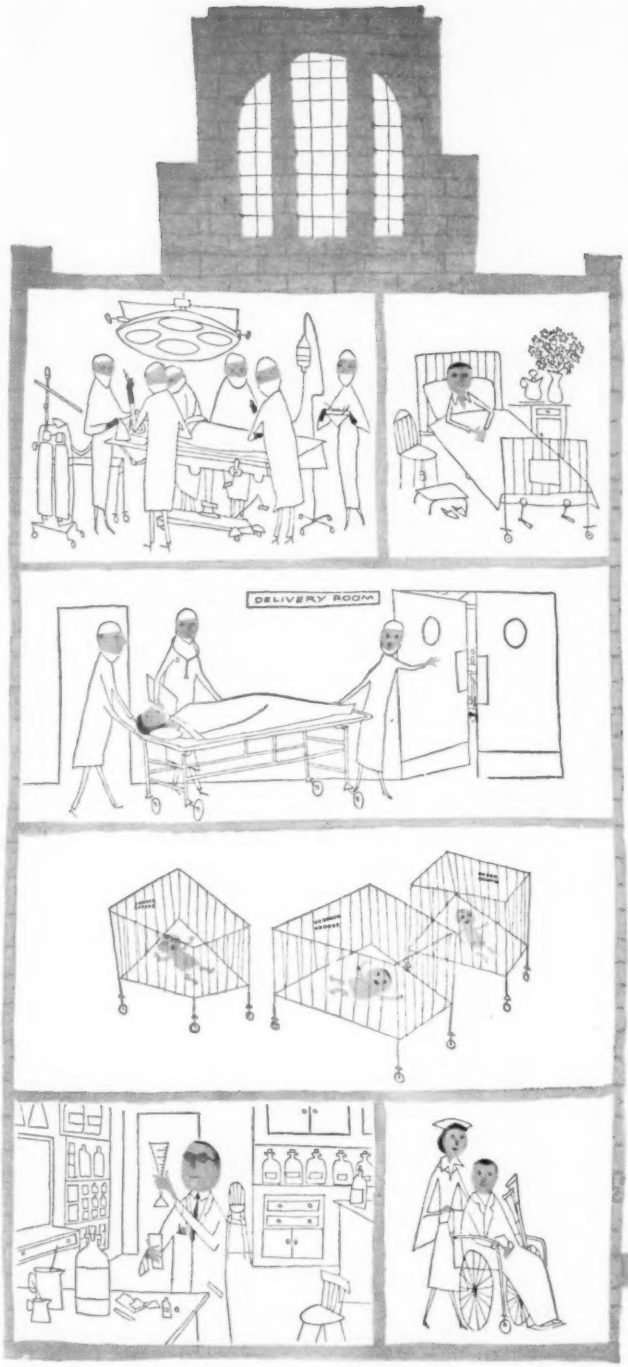
Capsules Potassium Aminosalicylate (Paskate) 0.5 Gm.
Powder Potassium Aminosalicylate (Paskalium).
Powder, Envelopes, Potassium Aminosalicylate (Paskalium Envules) 3 Gm.
Tablets Potassium Aminosalicylate (Paskalium) 0.5 Gm.

Selenium Sulfide

Use of Selenium Sulfide for Various Seborrheic Conditions

The Council has recognized the efficacy and relative safety for supervised external use of the sulfide of the systemically toxic element, selenium, in the treatment or control of seborrhea of the scalp. The agent is employed on the scalp as a suspension containing a concentration of 2.5%, which must be rinsed from the hair. It should be thoroughly washed from the hands and nails after application and kept away from the reach of children to avoid accidental ingestion and poisoning (New and Nonofficial Remedies 1955, pp. 618-619).

On the basis of further clinical and experimental investigations furnished by the manufacturer, the Council has evaluated wider external use of the drug as a 0.5% concentration in jelly form for seborrhea involving the eyebrows, eyelids (seborrheic blepharitis), the external auditory canal, and glabrous areas of the skin. Further studies indicate that concentrations above 0.5% may be too irritating for areas where the skin is thin, such as the eyelids. It has not been determined conclusively whether careless use or the concentration is chiefly responsible for



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Synkayvite is a water-soluble vitamin-K compound of high anti-hemorrhagic activity, assuring desired clinical results in obstetrics and surgery.

Synkayvite is convenient and time-saving. 5-mg (1 cc), 10-mg (1 cc) and 75-mg (2 cc) doses are all available in COLOR-BREAK ampuls which nurses open with a flick of the finger. Even the high-potency 75-mg dose is provided in low volume (2 cc).

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skin irritation; nor has it been established that 0.5% is the lowest concentration that is effective for use about the eyes, in the ear, or on the glabrous skin.

The Council sought opinions from several consultants in the fields of ophthalmology, otology, and dermatology concerning the available evidence. The ophthalmology consultants agreed that a 0.5% jelly is effective and essentially nonirritating for the treatment of seborrheic blepharitis but that caution is necessary to avoid accidental instillation into the conjunctival sac, which may produce a chemical keratitis and conjunctivitis. An otologist expressed the view that, in the external canal, the jelly form might be difficult to remove and that, because prolonged contact resulting from accumulation of the drug could increase the possibility of irritation, a more detailed clinical study should be made to determine whether a liquid preparation might be better suited for the ear. The 0.5% concentration otherwise was considered unlikely to cause irritation in the ear. The majority of dermatology consultants felt that the 0.5% jelly was suitable for use on the glabrous skin in the management of the dry, scaly form of seborrhea; but, because of the increased risk of cutaneous absorption in intertriginous, exudative, and acutely inflamed areas, it should not be applied in such forms of seborrheic dermatitis or to extensive areas of the skin. Some dermatologists also expressed the opinion that longer experience or controlled observations are needed to compare the effectiveness of selenium sulfide in chronic seborrheic dermatoses with established, less toxic agents.

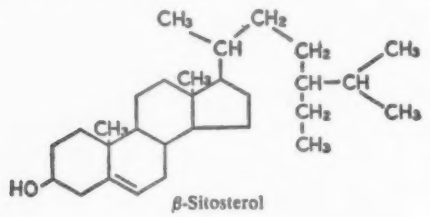
The Council concluded that judicious use of a jelly or other suitable preparations containing 0.5% or less of the drug was suitable for the management of noninflammatory, nonexudative seborrhea of the eyebrows, eyelids, external ear, and glabrous skin and voted to expand the New and Nonofficial Remedies monograph on selenium sulfide accordingly.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of selenium sulfide.

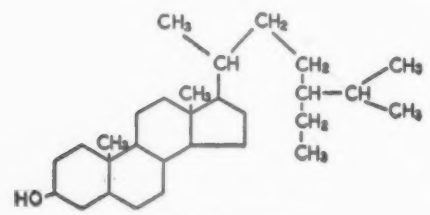
—J. Am. Med. Assoc. 160:51 (Jan. 7, 1956)

Sitosterols Cytellin®

SITOSTEROLS is a mixture of 80 to 90% β-sitosterol and 10 to 20% dihydro-β-sitosterol. The structural formulas may be represented as follows:



β-Sitosterol



Dihydro-β-Sitosterol

Actions and Uses

Sitosterols are closely related natural plant sterols that are chemically identical with cholesterol except for an ethyl group in the side chain and a saturated ring system in the dihydro derivative. They appear to enhance the fecal excretion of cholesterol, thus reducing blood cholesterol levels. Although the mechanism for this action is poorly understood, related sterols presumably interfere with the absorption of exogenous cholesterol contained in food and the reabsorption of endogenous cholesterol secreted in the bile and through the wall of the gastrointestinal tract.

Sitosterols have been proposed for use in conditions in which a sustained reduction of hypercholesterolemia is desirable. These would include conditions associated with hypercholesterolemia, such as diabetes mellitus, hypothyroid states, nephrosis, and xanthomatosis. Currently available evidence indicates that the drug is capable of reducing the level of circulating cholesterol in some patients; however, valid evidence is still lacking to indicate that the sitosterols produce beneficial effects in patients with existing atherosclerotic disease. Although additional long-term studies are necessary to evaluate the ultimate usefulness of the sitosterols in this respect, their ability to lower blood cholesterol levels warrants trial in selected cases; however, sitosterols should be administered only when it is possible for the physician to devote the extra time and attention necessary for evaluation of the long-term effects, including periodic determinations of blood cholesterol levels.

There have been no reports of toxic manifestations in animals or in patients to whom sitosterols have been administered for over 18 months. Since prolonged administration is involved, however, physicians should be alert for the appearance of any untoward symptoms.

The use of sitosterols in the management of hypercholesterolemia must be considered experimental at the present time. Since conclusive evidence of beneficial effects in the prevention or treatment of any disease is lacking, therapeutic trial of sitosterols is justified only on the basis of their apparent safety and the inadequacy of any other current form of therapy. Only subsequent clinical experience will determine its ultimate place in the therapeutic armamentarium against cardiovascular disease.

Dosage

Sitosterols are administered orally. The dosage should be individualized to produce the desired blood cholesterol response. The usual initial dose is 9 gm. per day, but doses as high as 36 gm. per day have been administered over prolonged periods without untoward effects. Since maximal efficiency of the sitosterols appears to depend upon their presence in the gastrointestinal tract at the time food is ingested, the daily dosage should be administered in divided amounts either before meals or before and after meals.

Preparations for use as stated for the foregoing drug are marketed under the following name: Cytellin.

Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of sitosterols.

—J. Am. Med. Assoc. 160:671 (Feb. 25, 1956)

Preparations

Suspension, Oral, Sitosterols (Cytellin) 3 Gm./15 ml.

Plant Sterols

In Hypercholesterolemia and Atherosclerosis

From statistical considerations, there is presumptive evidence that atherosclerotic cardiovascular disease is

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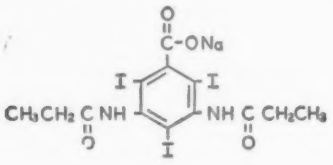
associated with prolonged hypercholesterolemia. Thus, atherosclerotic changes are frequently seen at autopsy in patients with diabetes mellitus, hypothyroidism, nephrosis, and familial xanthomatosis. All of these diseases are characterized by elevated blood cholesterol levels. In addition, the incidence of coronary heart disease and peripheral vascular disease is higher among such patients. This relationship, although statistically significant, is far from absolute. Patients are frequently encountered with clinically demonstrable cardiovascular disease in the presence of normal blood cholesterol levels. It is known, however, that atherosclerosis may be produced in laboratory animals by feeding them a diet high in cholesterol and that such changes may be reversed by resuming a more normal diet. Whether such changes occur in man is not known; however, such considerations would indicate that sustained reduction of circulating cholesterol levels appears to be desirable. This cannot be routinely accomplished by diets low in cholesterol, since a large part of the cholesterol in the body is formed by endogenous synthesis. Likewise, few patients adhere to low fat diets for sufficiently prolonged periods to evaluate adequately the effect of such a regimen on hypercholesterolemia. Administration of certain plant sterols represents a possible therapeutic means of effecting a reduction in blood cholesterol without rigid dieting.

In view of the eminence of cardiovascular disease as the foremost cause of death in this country and the inadequacy of all current means of therapy, interest in new forms of therapy that employ a positive approach is welcome. Whether reduction of hypercholesterolemia is the proper approach is conjectural at the present time.

—*J. Am. Med. Assoc.* *160*:670 (Feb. 25, 1956)

Sodium Diprotrizoate — Miokon® Sodium

SODIUM DIPROTRIZOATE is Sodium 3,5-dipropionamido-2,4,6-triiodobenzoate.—The structural formula of sodium diprotrizoate may be represented as follows:



Actions and Uses

Sodium diprotrizoate is employed as a contrast medium for intravenous (excretory) urography. The drug is transported rapidly to the kidneys and accumulates in the urine shortly after administration. For this reason, roentgenographic exposures are best made 5, 10, and 15 minutes after intravenous injection. When excretion is delayed by impaired renal function, it may be necessary to wait 30 minutes or longer before adequate roentgenographic shadows can be obtained. The density of the shadows is also influenced by the plasma iodine content and the concentration of the urine at the time of examination; thus, careful timing of exposures and restriction of pre-examination fluid intake is necessary for satisfactory pyelograms.

Side-effects of sodium diprotrizoate are similar to those produced by other contrast media of this type. Chief among these are nausea and vomiting, sweating and sense of intense warmth, urticaria, and pain in the injected arm. Serious cardiovascular side-effects are uncommon. The incidence of all types of reactions has been reported by various investigators to be between 10 and 15%. (See the general statement on water-soluble organic iodine compounds for roentgenography in New and Nonofficial Remedies.)

Dosage

For excretory urography, 20 to 30 cc. of a 50% solution is the usual intravenous dose for adults. A slow rate of injection (3 to 4 minutes) has been observed to decrease the incidence of side-effects. Before the full amount is injected, a "test dose" of about 1 cc. should be administered intravenously and the patient observed for signs of untoward reactions. Since aqueous solutions of sodium diprotrizoate are photosensitive, the drug should not be used after prolonged exposure to daylight.

Preparations for use as stated for the foregoing drug are marketed under the following name: Miokon Sodium.

Mallinckrodt Chemical Works cooperated by furnishing scientific data to aid in the evaluation of sodium diprotrizoate.

—*J. Am. Med. Assoc.* *160*:1143 (Mar. 31, 1956)

Preparations

Injection Sodium Diprotrizoate (Miokon) 50%; 30 ml. ampuls.

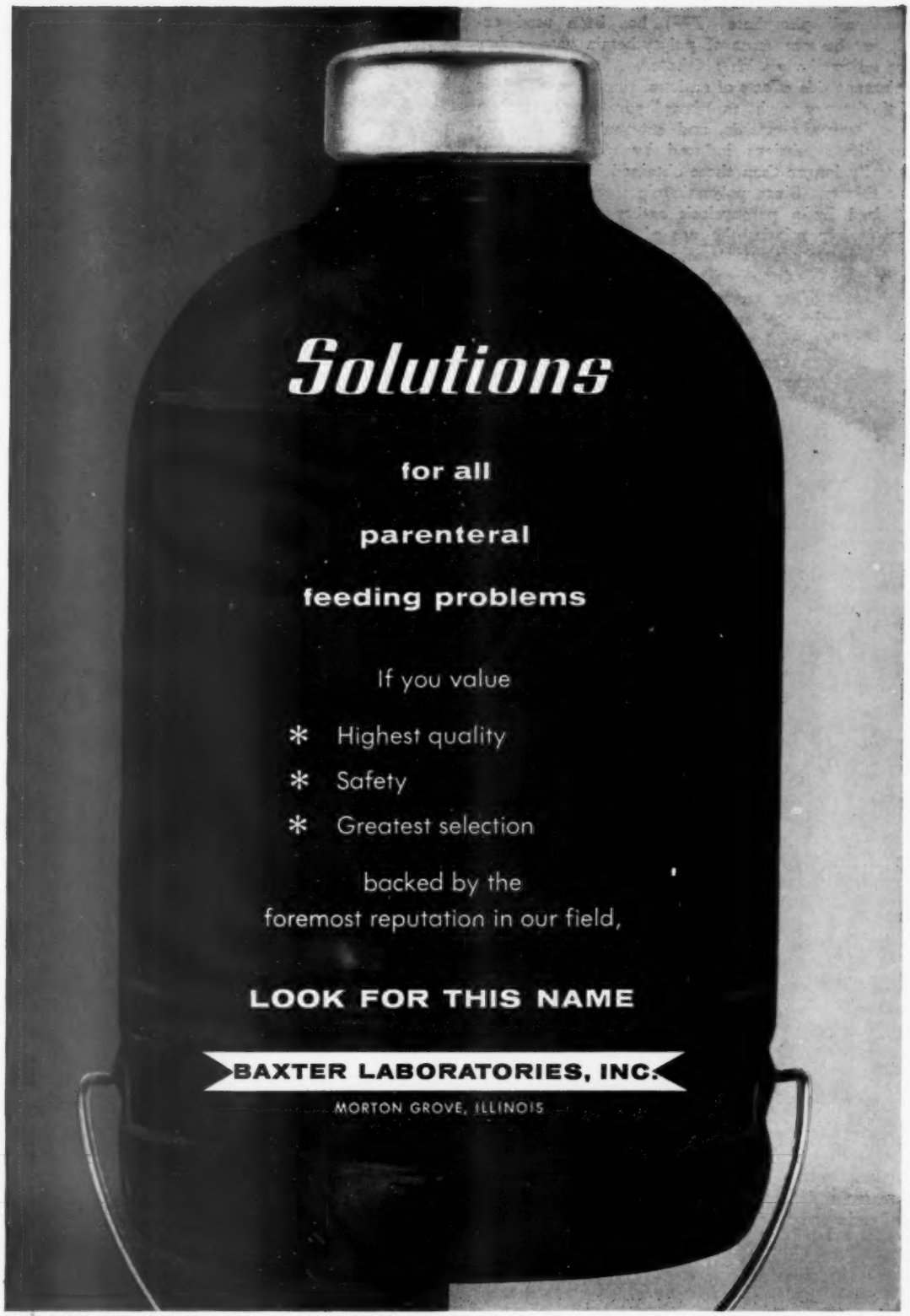
Sodium Radio-Phosphate (P^{32})

SODIUM RADIO-PHOSPHATE (P^{32}) is Anionic radioactive phosphorus in the form of a solution of sodium acid phosphate $NaHP^{32}O_4$ and sodium basic phosphate ($Na_2HP^{32}O_4$) having a pH between 5.0 and 6.0. It has a half-life of 14.3 days.

Actions and Uses

Sodium radio-phosphate (P^{32}) emits only beta particles, which dissipate a maximum energy of 1.69 million electron volts (mev) to a maximum depth of 8 mm. of tissue. Thus, most of the ionizing action is localized in the tissue that takes up the isotope. In the body, the radioisotope is metabolized in the same manner as stable phosphorus (P^{31}) and therefore is distributed to tissues in the same relative proportion as the stable element. After administration, the isotope is found in highest concentration in rapidly proliferating tissues with high phosphorus content such as bone marrow, lymph nodes, liver, and spleen. The distribution of radio-phosphorus is also influenced by disease, the uptake being much higher in neoplastic tissue than in the same type of tissue in a normal state of growth. Since the immediate uptake of the radioisotope is highest in those tissues that also exhibit the greatest radiosensitivity, its initial effects are similar to total body radiation; however, bone marrow ultimately becomes the most radioactive tissue regardless of initial distribution. The pharmacological effects of this isotope are related entirely to its local ionizing action, and the outstanding sequelae to overdosage are those resulting from bone marrow depression.

About 75% of the oral dose of sodium radio-phosphate (P^{32}) is absorbed from the gastrointestinal tract. After intravenous injection, the isotope rapidly enters the phosphate pool of the body and is distributed to the tissues. After either oral or intravenous administration, radio-phosphate is excreted in the urine, approximately



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25 to 50% of the drug appearing in the urine in the first 6 days.

Sodium radio-phosphate (P^{32}) has been used extensively in the treatment of polycythemia vera, either alone or adjunctively with phlebotomy. Its use obviates the unpleasant side-effects of and toxic reactions to older forms of therapy such as phenylhydrazine, potassium arsenite, nitrogen mustards, and external radiation. In addition, the remissions induced by radio-phosphorus are generally longer than those obtained by other drugs or x-ray therapy. Since polycythemia vera is frequently characterized by a panmyelosis rather than a simple erythrocytic hyperplasia, the use of an agent that depresses all marrow elements is particularly well suited for it therapy. Sodium radio-phosphate (P^{32}), in addition to controlling excessive erythrocyte levels, also depresses thrombocyte and leukocyte proliferation and thus reduces the incidental morbidity of arterial thrombosis and relieves the symptoms of hepatomegaly and splenomegaly. Although palliative, this agent is capable of inducing hematological remissions, leaving the patient symptom-free for months; however, its use is not without disadvantage. The chief disadvantage is the risk of excessive bone marrow depression with attending leukopenia, thrombocytopenia, and anemia. Frequent peripheral blood counts and, if necessary, bone marrow examinations are indicated for all patients undergoing radio-phosphorus therapy. Therapy should be discontinued should indications of excessive marrow depression become evident. Sodium radio-phosphate (P^{32}) is contraindicated for patients in whom the blood platelet count is less than 150,000, reticulocytes less than 0.2%, or white blood cell count less than 3,000.

Sodium radio-phosphate (P^{32}) has been used effectively in the treatment of chronic myelogenous leukemia. The internal radiations produced by the isotope are probably equally as effective as the external radiations produced by x-ray. Although radioactive phosphorus does not lengthen the survival time in chronic myelogenous leukemia, good hematological and clinical remissions have been obtained with its administration. Thus, it is considered one of the most effective therapeutic agents currently available for this disease. In chronic lymphocytic leukemia, sodium radio-phosphate (P^{32}) has been of some benefit, but the hematological and clinical response is not as good as that obtained by isotope therapy in the chronic myelogenous form of the disease. In many cases, local irradiation of affected lymph nodes brings more rapid relief of symptoms than does radio-phosphorus therapy. Acute leukemia, in any form, does not respond to therapy with radioactive phosphorus.

The drug is of little value in the treatment of Hodgkin's disease and is inferior to x-ray therapy in lymphosarcoma. It has not proved applicable in multiple myeloma nor in any solid tumors of carcinomatous or sarcomatous origin. The same precautions regarding bone marrow depression as are observed in cases of polycythemia vera should be exercised in treating chronic leukemia with radioactive phosphorus. Sodium radio-phosphate (P^{32}) should be administered with extreme caution to leukemic patients with red blood cell counts of less than 2,500,000.

Because of its preferential uptake in neoplastic tissues, sodium radio-phosphate (P^{32}) has been employed for the localization of brain tumors and for the diagnosis and localization of intraocular tumors. When the isotope is administered before surgery to patients with known intracranial tumors, it is sometimes possible to discern the extent of neoplastic involvement by means of probe counters applied directly to the exposed brain tissue. Although this procedure is reported to be useful in certain cases, it must be considered experimental at the present time. Because of the limited penetrating power of the emitted beta radiation, it is not possible to utilize the isotope for localization procedures unless the skull has been opened. Thus the drug fails to provide the preoperative information that can be obtained by established roentgenographic procedures. In addition, its use requires special equipment and must be reserved for experienced neurosurgeons trained in the use of radioisotopes.

In the diagnosis and localization of intraocular tumors, sodium radio-phosphate (P^{32}) is administered shortly before probe counters are placed over various areas of the same eye or symmetrically located areas of both eyes. Increased radioactivity over any particular area may be presumptive evidence of neoplastic involvement. Unlimited experience has indicated the procedure to be of some value in the diagnosis and localization of anterior tumors but of little value in more deep-seated intraocular malignancies. Although the isotope may be employed in conjunction with routine ophthalmologic procedures, the requirement for special equipment and trained personnel has restricted its clinical use. Until more experience is attained, therefore, the use of this agent in ophthalmology must be considered experimental.

While the use of sodium radio-phosphate (P^{32}) for tagging red blood cells for a single blood volume determination is no less accurate, the use of other radio-active agents, such as sodium radio-chromate (Cr^{51}), provides longer term tagging and is now considered preferable for this purpose. The isotope is extensively used in experimental laboratories as a metabolic tracer.

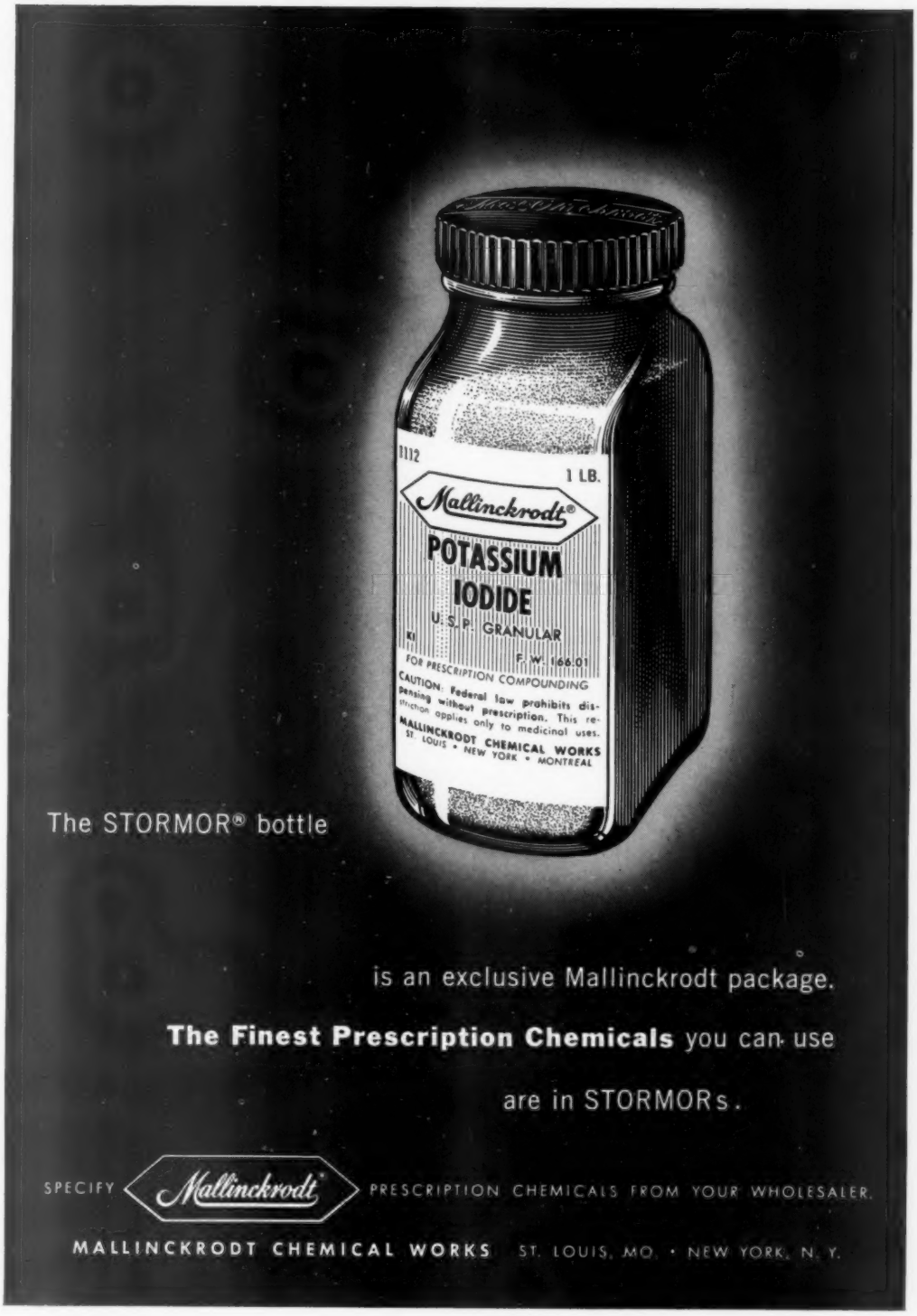
Although the isotope as supplied in glass containers is relatively safe, extreme care should be observed in handling. Severe beta radiation burns can result from contact with the skin. The radioactive material should be handled only by personnel well trained in the use of radioisotopes, and adequate monitoring apparatus should be available at all times.

Dosage

Sodium radio-phosphate (P^{32}) dosage calculations must take into account radioactive decay. Radioactive phosphorus has a half-life of 14.3 days, and the radioactivity, expressed as microcuries or millicuries, is indicated at the time of labeling. The isotope is administered orally or intravenously in aqueous solutions of appropriate concentration.

In polycythemia vera, initial intravenous doses vary from 2.5 to 5 mc. (millicuries) depending on the severity of the disease. The average initial dose is 3 mc. Phlebotomy may be carried out prior to isotope therapy to reduce the erythrocyte count to 6,000,000 or the hematocrit value to 55%. Hematological examinations should be carried out at bimonthly intervals after therapy. If at the end of two or three months further treatment is indicated, an additional dose may be given at that time, not to exceed 3 or 4 mc. Repeat doses should be given at intervals of not less than two months. Because of incomplete absorption, oral doses must be increased 25% over intravenous doses.

Chronic leukemias (myelogenous and lymphatic) are treated with repeated low doses of sodium radio-phos-



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phate (P^{32}). Treatment must be individualized because of great variations in response. For the average patient, 1 to 2 mc. intravenously each week for four to eight weeks is usually necessary to bring about remissions. Patients should be examined each week during this initial period, with particular emphasis being placed on the trend of blood cell response and the general clinical picture. If remissions occur, monthly examinations should be carried out and subsequent courses of therapy instituted when clinical signs and symptoms recur. It may be possible to maintain patients in remission by carefully arriving at the minimum dose that will keep the white blood cell count between 10,000 and 20,000. Experience has shown that it is not advisable to attempt to adjust the blood elements to normal levels, because of the danger of overdosage. Oral doses are increased proportionately to overcome incomplete absorption.

For brain tumor localization, 0.5 to 1 mc. of sodium radio-phosphate (P^{32}) is injected intravenously 12 to 24 hours before surgery. In the diagnosis and localization of intraocular tumors, 0.5 mc. intravenously is the proposed dose.

Preparations for use as stated for the foregoing drug are marketed under the following name: Sodium Radio-Phosphate (P^{32}).

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of sodium radio-phosphate (P^{32}).
—*J. Am. Med. Assoc.* *160*:669 (Feb. 25, 1956)

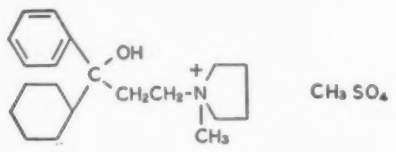
Preparations

Injection Sodium Radio-Phosphate (P^{32}) 1 to 100, or more, millicuries/vial.

Tricyclamol Methylsulfate

Elorine® Methylsulfate

TRICYCLAMOL METHYLSULFATE is 1-Cyclohexyl-1-phenyl-3-pyrrolidino-1-propanol dimethylsulfate.—The structural formula of tricyclamol methylsulfate may be represented as follows:



Actions and Uses

Tricyclamol methylsulfate is an anticholinergic agent qualitatively similar in action to other drugs of that class. Available evidence indicates it is less effective in reducing secretory activity than hypermotility of the gastrointestinal tract and that the drug offers no advantage over other anticholinergic drugs such as methantheline and methscopolamine from the standpoint of over-all effectiveness, toxicity, or side effects.

Tricyclamol methylsulfate may be employed clinically for the control of functional spasm of the gastrointestinal tract as an adjunct in the treatment of peptic ulcer, chronic gastritis associated with hyperacidity, pylorospasm, and irritable colon (mucous, spastic colitis). In these conditions it should be borne in mind that antispasmodic therapy may be less important than dietary restrictions and the use of sedative or antacid medication. Its value in the management of regional ileitis and ulcerative colitis, or for other purposes, has not been established.

Tricyclamol methylsulfate may produce atropine-like side-effects characteristic of anticholinergic agents. Mouth dryness is most commonly encountered at therapeutically effective dosage levels. Occasional paralysis of ocular accommodation and infrequent difficulty in urination have been observed. As with other anticholinergic agents, the drug usually is contraindicated in glaucoma and should be employed with caution in patients with cardiac decompensation or coronary insufficiency, cardiospasm or achalasia, unrelieved duodenal obstruction, and prostatic hypertrophy or bladder neck obstruction. One case of psychosis resulting from toxic reaction to the drug requires further investigation. Until longer experience has been gained, physicians should be alert to the possible development of serious untoward effects that may result from continued use of the drug.

Dosage

Tricyclamol methylsulfate is administered orally. Individual requirements for this drug vary widely, ranging between 50 and 500 mg., and averaging 100 to 150 mg. It is suggested that patients be started on a trial dosage of 50 mg. four times a day. This should be increased until a satisfactory response is obtained or the individual's tolerance is reached. The frequency of administration may be increased to six time a day, if indicated.

Preparations for use as stated for the foregoing drug are marketed under the following name: Elorine Methylsulfate.

Eli Lilly & Company cooperated by furnishing scientific data to aid in the evaluation of tricyclamol methylsulfate.
—*J. Am. Med. Assoc.* *160*:467 (Feb. 11, 1956)

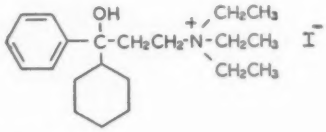
Preparations

Capsules Tricyclamol (Elorine) Methylsulfate 25 mg. and 50 mg.

Tridihexethyl Iodide

Pathilon® Iodide

TRIDIHEXETHYL IODIDE *is* 3-Diethylamino-1-phenyl-1-cyclohexyl-1-propanol ethiodide.—The structural formula of tridihexethyl iodide may be represented as follows:



Actions and Uses

Tridihexethyl iodide, an aminopropanol compound chemically related to trihexyphenidyl hydrochloride and cycrimine hydrochloride, is a synthetic anticholinergic drug with pharmacological actions similar to other drugs of this class. In therapeutic doses, it produces more of the peripheral action of cholinergic blocking agents such as atropine than the ganglionic blocking action of drugs such as tetraethylammonium chloride. Its therapeutic effectiveness as well as its side-effects therefore can be attributed primarily to its atropine-like action.

Tridihexethyl iodide is useful as an adjunct in the treatment of peptic ulcer, gastric hyperacidity and hypermotility, gastrointestinal spastic conditions such as spastic and irritable colon, functional diarrhea, pylorospasm and hypermotility of the small intestine that is not associated with organic change. The drug may also be employed in selected cases of gastritis in which the symptoms are caused by hyperacidity. Its use as a postoperative spasmolytic agent has not been established.

ACTH
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One injection is effective for 24 to 72 hours or more

By adsorption of ACTH on zinc hydroxide, Cortrophin-Zinc permits extension of ACTH activity for a period of 1 to 3 days. This minimizes the therapeutic "ups and downs" which may occur during ACTH-in-gel therapy and provides smooth corticotropin action for a truly extended period.

Cortrophin-Zinc is easier to handle than gelatin preparations. An aqueous suspension, it flows easily through a 26-gauge needle, eliminating preheating, clogging syringes, and heavy-gauge needles that add to the pain.

Cortrophin-Zinc is supplied in 5 cc vials each cc containing 40 U.S.P. units of corticotropin with 2 mg. of zinc.

CORTROPHIN* ZINC†

a development of **Organon Inc.**
ORANGE, N. J.

*T.M.—Cortrophin Available in other countries as Cortrophine-Z †Patent Pending

The incidence and severity of side-effects resulting from tridihexethyl depend chiefly on the size of the dosage. Because of its predominant peripheral atropine-like actions, the drug in well-tolerated orally given doses is more effective in decreasing gastric hyperacidity than gastric hypermotility and gastrointestinal spasticity. When administered intravenously, the effect on gastric hypermotility and gastrointestinal spasm is increased. To be effective in the latter conditions, the orally given doses must generally be increased until mild side-effects appear, or the drug may be given parenterally in smaller doses. As with other anticholinergic drugs, tridihexethyl iodide produces blurring of vision, dryness of the mouth, tachycardia, and urinary retention. These side-effects are frequently not severe enough to warrant discontinuance of the drug, but patients should be advised of the possible appearance of such symptoms. In the therapeutic range of doses, severe toxic reactions are infrequent. Should these occur, suitable cholinergic agents such as neostigmine are indicated. Since tridihexethyl iodide produces some degree of mydriasis, it should not be administered to patients with glaucoma. It should be administered cautiously to patients with cardiac decompensation or coronary insufficiency. It is contraindicated in patients with obstruction at the bladder neck, prostatic hypertrophy, stenosing gastric and duodenal ulcers, or pyloric or duodenal obstruction.

Dosage

Tridihexethyl iodide is administered orally or by subcutaneous, intramuscular, or intravenous injection. Because the drug is less well absorbed orally than parenterally, the orally given dose must be larger than the parenterally given dose in order to achieve the same therapeutic effect. The suggested dosage for oral administration for adults is 25 to 50 mg. three or four times a day for most uncomplicated cases of peptic ulcer; however, in some severe or complicated cases, a dosage in excess of 100 mg. every 6 hours may be required. This higher dosage may induce atropine-like side-effects. The physician must therefore individualize the orally given dose according to the severity of the condition and the appearance of side-effects. In the average patient, smaller doses are effective when the drug is administered intravenously. The suggested dosage for parenteral administration is 10 to 20 mg. every 6 hours, but oral therapy should be substituted as soon as the patient can tolerate medication by that route.

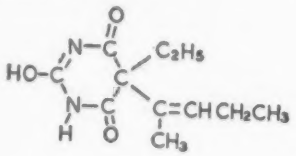
Preparations for use as stated for the foregoing drug are marketed under the following name: Pathilon Iodide.
Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of tridihexethyl iodide.
—*J. Am. Med. Assoc.* *160*:389 (Feb. 4, 1956)

Preparations

Injection Tridihexethyl (Pathilon) Iodide 10 mg./ml.; 1 ml. ampuls.
Tablets Tridihexethyl (Pathilon) Iodide 25 mg., coated.

Vinbarbital N.F. Delvinal®

VINBARBITAL, N. F. is 5-Ethyl-5(1-methyl-1-butenyl)-barbituric acid. The structural formula of vinbarbital may be represented as follows:



Actions and Uses

Vinbarbital, a barbituric acid derivative with intermediate duration of action, has the same sedatve and hypnotic uses as its sodium salt. (See the monograph on vinbarbital sodium in New and Nonofficial Remedies.) Its use involves the same side-effects as other barbituric acid derivatives, but it is less likely to cause epigastric distress after oral administration than the sodium salt.

Dosage

See the monograph on vinbarbital sodium in New and Nonofficial Remedies.

Preparations for use as stated for the foregoing drug are marketed under the following name: Delvinal.
Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of vinbarbital.
—*J. Am. Med. Assoc.* *160*:671 (Feb. 25, 1956)

Preparations

Capsules Vinbarbital (Delvinal) 30 mg., 100 mg., and 200 mg.
Elixir Vinbarbital (Delvinal) 0.25 Gm./30 ml.
Injection Vinbarbital (Delvinal) 60 mg./ml.; 5 ml. ampuls and 20 ml. vials.

Xanthines

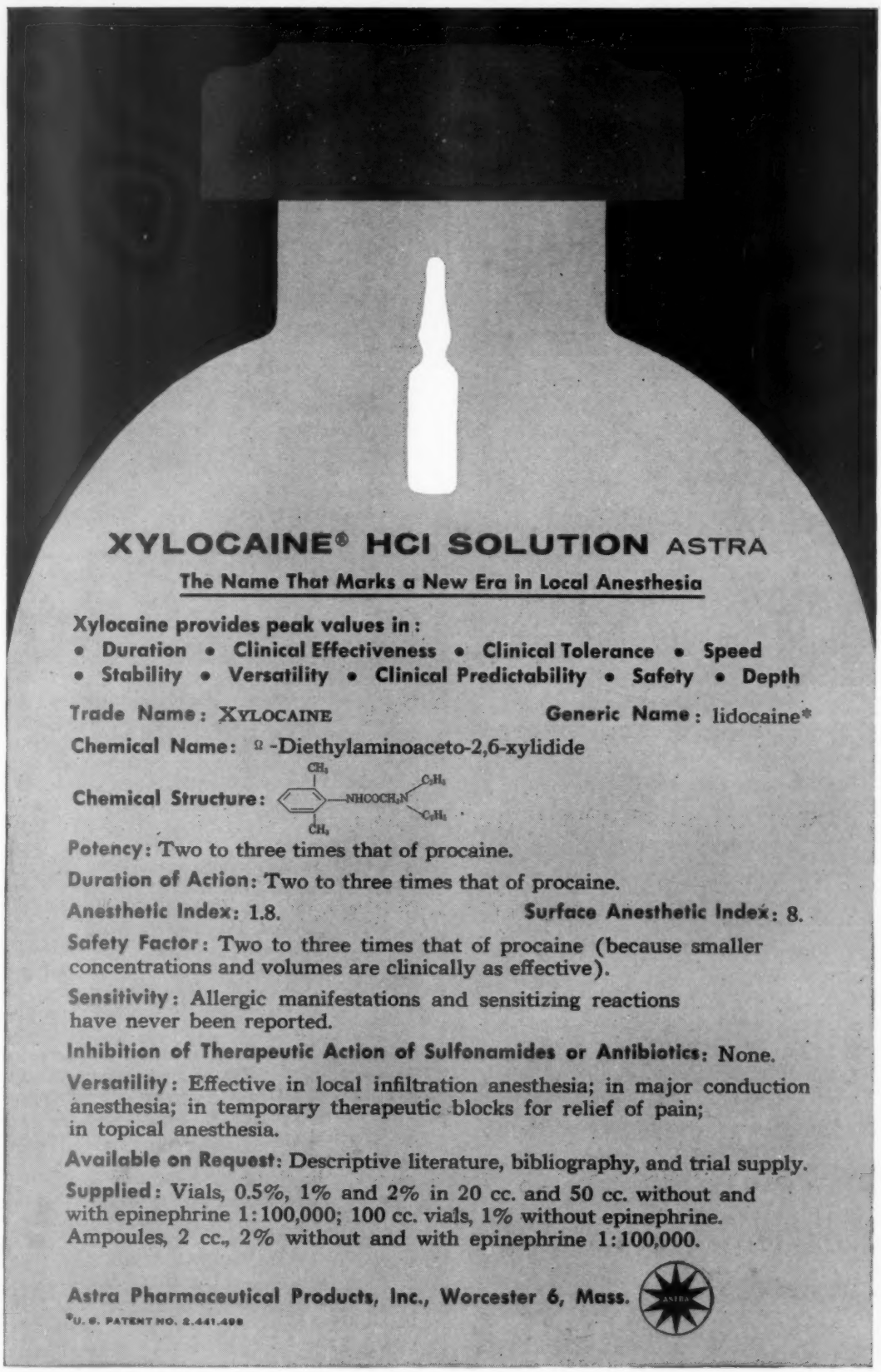
Use of Xanthine Derivatives in Coronary Disease

Xanthine derivatives, other than caffeine, are frequently used clinically as vasodilators in angina pectoris and coronary disease to increase coronary blood flow. Caffeine is seldom used except as a central nervous system stimulant. For several years the Council has maintained a critical attitude toward the use of theobromine or theophylline compounds for coronary heart disease because the increased coronary blood flow follows rather than precedes stimulation of the myocardium by xanthine. The latter effect also may be undesirable in patients with angina. Thus, although the ability of compounds such as aminophylline to increase coronary circulation in experimental animals is well established, the Council has withheld recognition of the clinical use in coronary disease.

Recently in reviewing the status of aminophylline and other theophylline compounds, the Council again was informed of the conflicting clinical reports on their effectiveness in coronary disease. Some clinics have found their use beneficial, whereas others, using placebos for comparison have obtained negative results. It was also apparent that competent clinicians had infrequently observed some beneficial effect in diminishing the frequency of attacks of angina in certain patients. The Council concluded that, although the clinical evidence was inconclusive and the potential benefit slight, theobromine or theophylline compounds could be tried in selected cases whenever myocardial stimulation would not be harmful. It was further indicated that compounds that are not tolerated orally in adequate doses because of gastric irritation should be administered parenterally.

The Council voted to amend New and Nonofficial Remedies accordingly to recognize the limited use of xanthine derivatives (other than caffeine) in angina pectoris and coronary disease.

—*J. Am. Med. Assoc.* *160*:51 (Jan. 7, 1956)



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Xylocaine provides peak values in:

• **Duration** • **Clinical Effectiveness** • **Clinical Tolerance** • **Speed**
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Trade Name: XYLOCAINE **Generic Name:** lidocaine*

Chemical Name: α-Diethylaminoaceto-2,6-xylidide

Chemical Structure:

Potency: Two to three times that of procaine.

Duration of Action: Two to three times that of procaine.

Anesthetic Index: 1.8. **Surface Anesthetic Index:** 8.

Safety Factor: Two to three times that of procaine (because smaller concentrations and volumes are clinically as effective).

Sensitivity: Allergic manifestations and sensitizing reactions have never been reported.

Inhibition of Therapeutic Action of Sulfonamides or Antibiotics: None.

Versatility: Effective in local infiltration anesthesia; in major conduction anesthesia; in temporary therapeutic blocks for relief of pain; in topical anesthesia.

Available on Request: Descriptive literature, bibliography, and trial supply.

Supplied: Vials, 0.5%, 1% and 2% in 20 cc. and 50 cc. without and with epinephrine 1:100,000; 100 cc. vials, 1% without epinephrine. Ampoules, 2 cc., 2% without and with epinephrine 1:100,000.

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Separate packaging of dry vitamins and diluent (mixed immediately before injection) assures the patient a more effective dose. May also be added to standard IV solutions.

Dosage: 2 cc. daily.

Each 2 cc. dose contains:

Thiamine HCl (B_1)	10 mg.
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Niacinamide	50 mg.
Pyridoxine HCl (B_6)	5 mg.
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Vitamin B_{12}	15 mcgm.
Folic Acid	3 mg.

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Report to the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

In July, 1954, the Subcommittee on Blood Dyscrasias established a registry in the headquarters office of the Committee on Research for the reporting of blood dyscrasias caused by toxic agents. Since that time, 33 cooperating hematologists have reported 110 cases of blood dyscrasia that they considered to be caused by various drugs and toxic chemicals. A review of this series revealed that nine of the cases reported were associated with the use of the new drug chlorpromazine. Since the main purpose of the registry is to warn physicians at the earliest possible moment of the occurrence of blood dyscrasias coincident with the use of newly introduced drugs, it was felt important to call this fact to the attention of the medical profession.

NORMAN DE NOSAQUO, M.D., *Secretary*
Committee on Research

Chlorpromazine

Blood Dyscrasias Associated with Chlorpromazine Therapy

A review of the reports received from cooperating hematologists since July, 1954, first revealed nine cases of blood dyscrasia associated with chlorpromazine therapy. A search of the literature has revealed six additional cases reported in American and British literature to the date of preparation of this report. Through the cooperation of Smith, Kline & French Laboratories, 32 other cases occurring in the United States were added, making a total of some 45 reported cases of blood dyscrasias coincident with chlorpromazine therapy. It should be emphasized that in many instances other drugs also had been given. As with reports of any such clinical association, the evidence is circumstantial rather than final but may nevertheless be significant.

Smith, Kline & French Laboratories have estimated that approximately 4 million people in the United States have been exposed to chlorpromazine since its introduction. Although it must be assumed that not all cases of blood dyscrasia associated with the drug have been reported, the indications are that the rate of incidence of blood dyscrasia is low, involving possibly only 1 in 50,000 to 100,000 patients receiving the drug (0.002 to 0.001%).

The blood dyscrasia most often reported was agranulocytosis, although in many cases bone marrow studies revealed depression of other cellular elements as well as the granulocyte precursors. In 17 patients in whom this condition appeared the outcome was fatal; however, in cases recognized early, recovery generally followed cessation of chlorpromazine administration.

Physicians who prescribe chlorpromazine should instruct their patients to report at once any sudden occurrence of sore throat or other signs of reaction. Differential blood cell counts should be done routinely; however, since the onset of this condition may be sudden and since the disease may develop fully before the patient reports to the physician, routine blood cell counts cannot be relied upon as the sole criterion for agranulocytosis. Because of this possibility the patient must be warned to be alert to any change.

Smith, Kline & French Laboratories have included this type of warning rather prominently in their literature, and they should be commended for their wholehearted cooperation with the Subcommittee. The Subcommittee suggests that, since the drug appears to possess a potential for some harm, it should be recommended that physicians limit its use to those conditions in which such use is warranted and avoid its use in the treatment of trivial or minor complaints.

—*J. Am. Med. Assoc.* **160**:287 (Jan. 28, 1956)

LETTERS

Comments on Annual Meeting

DEAR SIRS: . . . We all came away from the Annual Meeting in Detroit with the feeling that it was most successful. I am looking forward to next year already.

JOHN A. SCIGLIANO, *President*
Maryland Association of Hospital Pharmacists.
Bethesda, Md.

DEAR SIRS: I would like to say that I thoroughly enjoyed this past Convention in Detroit. The meetings were very good and the idea of presenting each delegate with copies of the reports was helpful.

I would like to make two suggestions. First, that members of the SOCIETY OF HOSPITAL PHARMACISTS wear flyers attached to their name cards, such as those worn by members of some of the other affiliated groups. This would indeed make our group distinctive and since there are many members of the ASHP who do not know or recognize fellow members, this would surely help. The second suggestion is that the institution or company with which a member is associated be designated on each name card. The advantage of this suggestion is readily apparent.

. . . Thank you for your interest and cooperation.

LOUIS P. JEFFREY, *Pharmacist-in-Chief*
Albany Hospital
Albany, N. Y.

From Saudi Arabia

DEAR SIRS: Enclosed please find checks covering membership in the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. I find the Journals and THE BULLETIN of even greater value here in Saudi Arabia than ever before.

FREDERICK M. MCKINNEY, *Pharmacist*
Arabian American Oil Company
Dhahran, Saudi Arabia

Appreciation

DEAR SIRS: The Texas Society of Hospital Pharmacists at one of its Annual Meetings in Austin in February, passed the following resolution:

Whereas THE BULLETIN contributed generously toward the program by giving the Eighth Annual Hospital Pharmacy Seminar advance publicity, therefore,

Be it resolved that this Chapter extend its appreciation and thanks to the Editorial Staff of this publication.

LOUISE POPE, *Secretary*
Texas Society of Hospital Pharmacists
University of Arkansas Medical Center
Little Rock, Ark.

DEAR SIRS: Thank you very much for the reprint, "Radioisotopes in Hospital Pharmacy," from THE BULLETIN OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

J. GUASCH

Instituto Policlinico
Platón, l-Barcelona

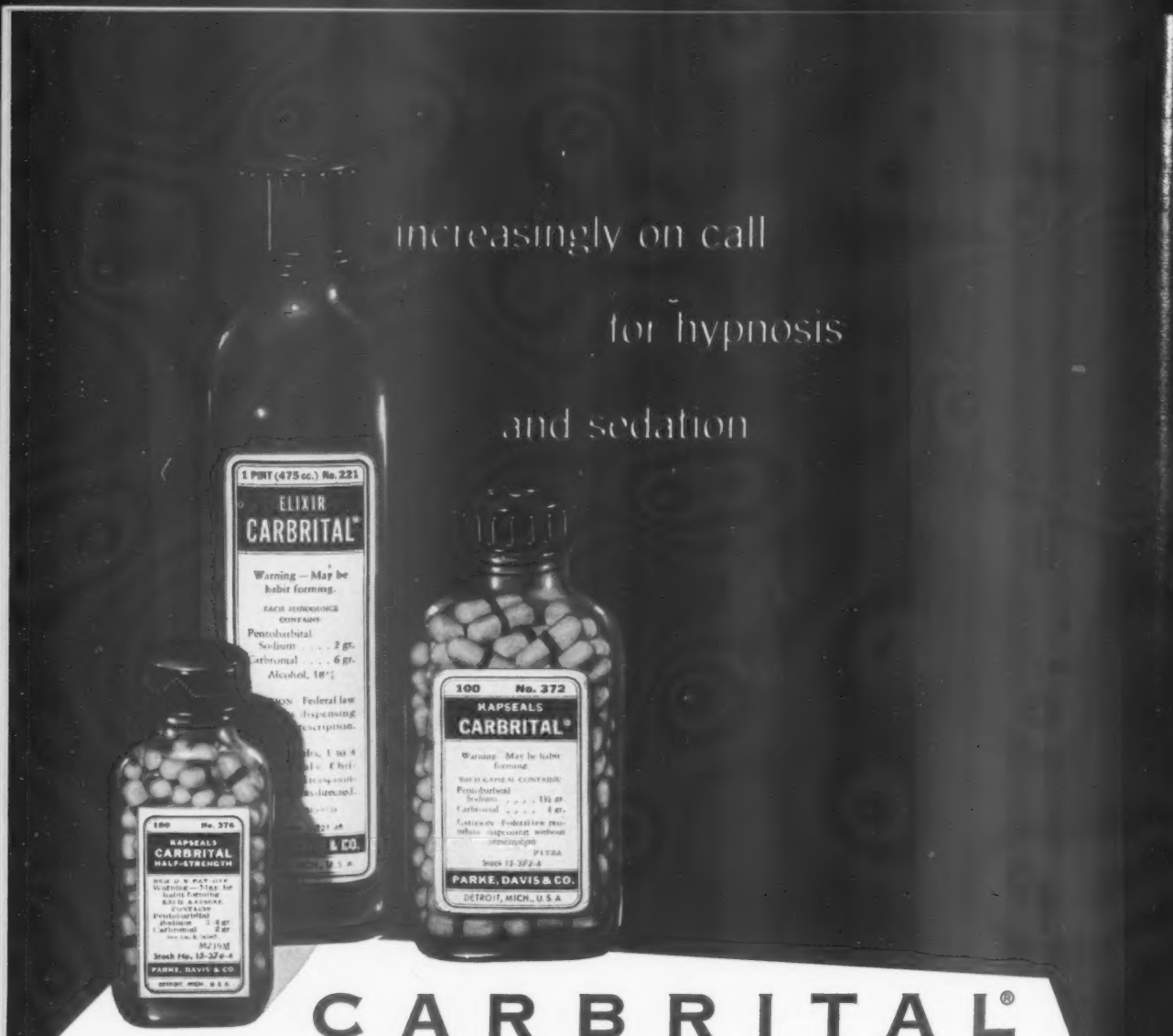
Information Requested

Dear Sirs: As a long time member of the SOCIETY and a reader of our publication, I have noted with interest the proposed Formulary Service. The project sounds definitely valuable to all hospitals. At the present time, however, this hospital is making plans for a proposal of a Pharmacy and Therapeutics Committee with the idea of starting work on a Formulary. Any help you may be able to give will be appreciated. In the past you have been willing to loan typical formularies to interested parties. Would you be kind enough to send a few representative ones to us? If you could include one from a tuberculosis hospital, it would be valuable. Also, any reprints on Committee selection, organization, etc. might be included if possible. We are now working out the procedure and I have gained some information through the pages of THE BULLETIN and other professional journals. We will be glad to pay any charges.

Also, do you have information as to source of supply of a heavy duty mixer suitable for making ointments in small quantities (under five pounds). All the commercial ones listed are very expensive mills or mixers for large scale manufacture.

Thank you so much. I find my membership in the A.Ph. A. and the ASHP at both the local and national levels valuable.

ZENNIE M. STAUFFER, *Pharmacist*
State of Oregon
Tuberculosis Hospital
Salem, Ore.



CARBRITAL®

In the hospital, CARBRITAL continues to demonstrate its particular advantages in combating the ever-present problem of insomnia. It provides two stage hypnotic-sedative effect of short-acting pentobarbital sodium and milder, longer-lasting carbromal. Restless patients are helped to fall asleep promptly and to stay asleep throughout the night, without likelihood of morning "hangover."

CARBRITAL is well adapted to preoperative and to postoperative uses, and is especially valuable in obstetrical care and during blood transfusions, special examinations, and other procedures, in which its hypnotic-sedative action helps to minimize initial pain and to allay subsequent discomfort.

packaging: CARBRITAL Kapseals®—pentobarbital sodium, 1½ gr., and carbromal, 4 gr. In bottles of 100 and 1,000. CARBRITAL Kapseals (Half-Strength)—pentobarbital sodium, ¾ gr., and carbromal, 2 gr. In bottles of 100 and 1,000. CARBRITAL Elixir—pentobarbital sodium, 2 gr. per fluidounce (¼ gr. per teaspoonful), carbromal, 6 gr. per fluidounce (¾ gr. per teaspoonful). In 16-ounce bottles.

dosage: Adults: 1 or more Kapseals as required; or 1 to 4 teaspoonfuls of the Elixir as required. *Children:* ½ to 1 teaspoonful according to age and condition.

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EDITORIAL

New and Nonofficial Remedies 1956

by Don E. Francke

No longer are drugs *accepted* by the Council on Pharmacy and Chemistry of the American Medical Association for publication in *New and Nonofficial Remedies*. Rather, drugs contained in the 1956 *N.N.R.* are those which have been *evaluated* by the Council. This change from *acceptance* to *evaluation* represents, in essence, the basic difference in operating policy used in preparing monographs for the new *N.N.R.* Thus the 1956 edition of the *N.N.R.* incorporates for the first time in book form the new revised program which the Council on Pharmacy and Chemistry initiated during 1955 (see BULL. AM. SOC. HOSP. PHARM. *12*:522, Sept.-Oct., 1955). This important revision of policy should be known and understood by hospital pharmacists, physicians, and others who are concerned with the status of drugs.

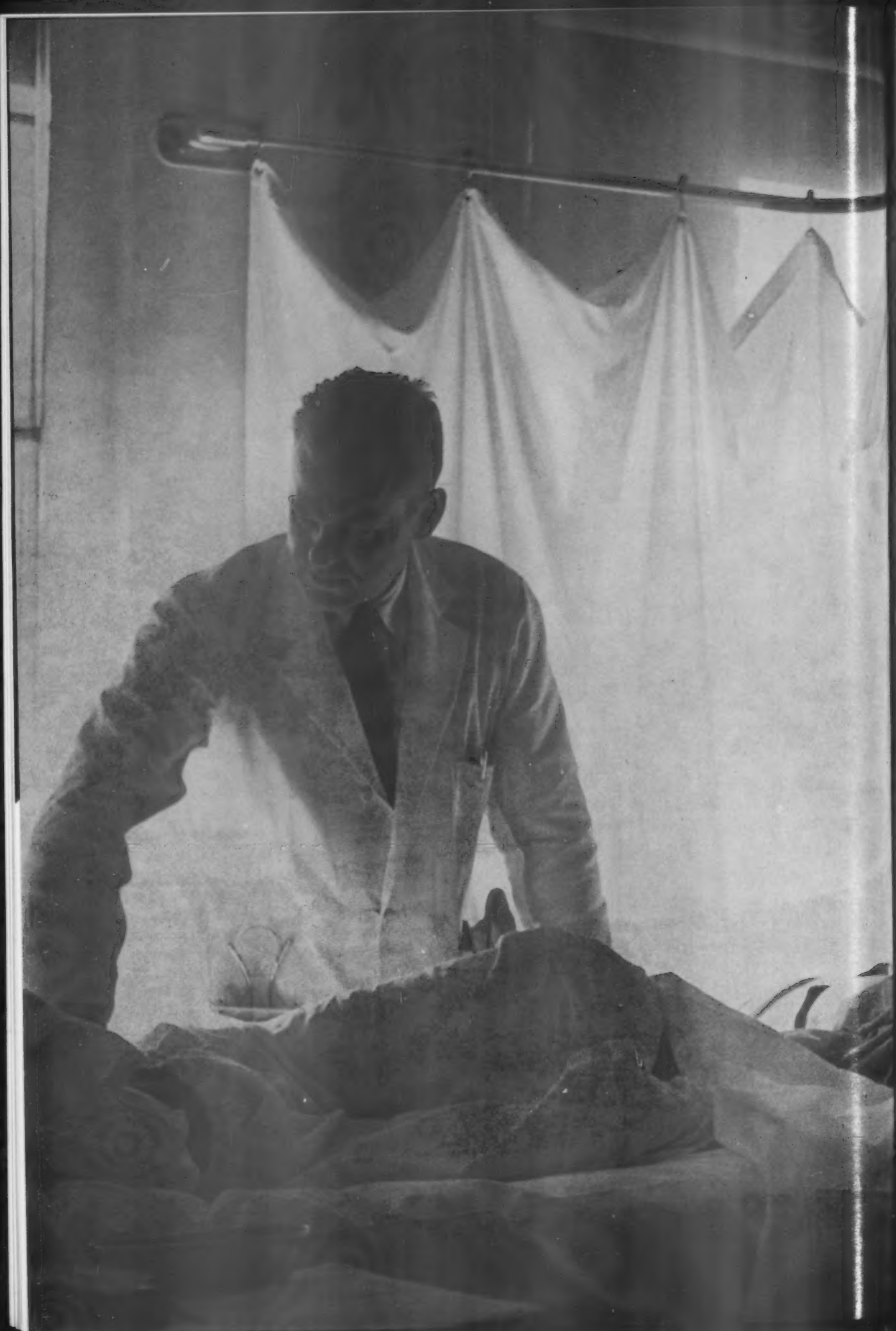
Under the new evaluation program greater emphasis is placed upon new drugs and currently available information is published in monograph form. These monographs represent an evaluation and summary of currently available evidence which, of course, is subject to change or modification. Thus the monographs reflect the current status of the drugs based upon available evidence, whether or not this information is sufficient to determine the ultimate importance or usefulness of the drugs. This prompt publication of evaluations means that physicians and pharmacists have unbiased reports on new drugs available to them at an early date. All concerned with drugs welcome this service.

Another feature of the new program is periodic publication of supplemental statements concerning evaluated new uses, routes of administration, or significant changes in the therapeutic status of previously evaluated drugs. These timely supplements greatly enhance the evaluation program which is published as a regular feature in *The Journal of the American Medical Association.*

A point of difference between the 1956 *N.N.R.* and prior editions is the omission of information on commercial dosage forms and package sizes of the drugs described. This information is being omitted since it is available from the distributors of the drugs and from other sources, and in order that the Council on Pharmacy and Chemistry may devote more time to evaluations of drugs. However, trade names of the drugs are listed in conjunction with the monographs. As the drugs become available from additional manufacturers, new trade names will be added to future editions of the book.

Neither are mixtures of drugs evaluated in the new *N.N.R.*; rather, the emphasis is placed almost entirely on the evaluation of individual drugs. It is expected, however, that physicians will be more readily able to evaluate combinations of drugs when they have information on the component individual drugs available to them at an early date.

Because of the great usefulness of current, objective evaluations of new drugs to hospital pharmacists, the drug monographs as published periodically in *The Journal of the American Medical Association* are now being carried in THE BULLETIN (see page 163). In order to make this information even more valuable, and to adapt it to the special needs of hospital pharmacists, dosage forms and preparations of the drugs have been added. In general, each issue of THE BULLETIN will carry monographs published over the course of eight weeks in *J.A.M.A.* For convenience, the drugs included in each issue will be indexed. Hospital pharmacists will undoubtedly find this material of significant value to them in their work with their Pharmacy and Therapeutics Committees, in the teaching of student nurses, supplying information to the medical, nursing, and allied staffs, and in other responsibilities where information on new drugs is essential.



THE DRUG EVALUATION PROGRAM

by H. D. KAUTZ

A SIGNIFICANT CHANGE IN METHOD of operation was instituted in February 1955 by the A.M.A. Council on Pharmacy and Chemistry to improve and expand its basic program for the evaluation of drugs. This change in program was the subject of a subsequently published statement (Council on Pharmacy and Chemistry: New Program of Operation For Evaluation of Drugs, *J.A.M.A. 158*:1170-1171, July 30, 1955)* and has superseded entirely the rules governing the former seal-acceptance program. The statement redefines the general purpose of the Council and outlines the governing principles and specific procedure under which drugs currently are evaluated and described in its annual publication, *New and Nonofficial Remedies* (*N.N.R.*) Revision of this well-known Council publication, to bring it in conformity with the revised method of drug evaluation, was implemented during 1955 by appropriate change of format in the N.N.R. section of the Council's column of *The Journal of the American Medical Association* and reflects the altered context of the book.

H. D. KAUTZ, M. D. is Secretary of the Council on Pharmacy and Chemistry, American Medical Association, Chicago, Ill.

Presented at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Detroit, Mich., April 10, 1956.

**See also* BULL. AMER. SOC. HOSP. PHARM. *12*:522 (Sept.-Oct.) 1955.

New Plan Of Drug Evaluation

The Council's function as a scientific drug-evaluating body for over fifty years, and its annual publication of *New and Nonofficial Remedies* since 1907, as a source of unbiased information on drugs, have become widely known throughout medicine, pharmacy and allied professional groups. It is not therefore surprising that the institution of a fundamentally different plan of drug evaluation in 1955 has aroused scientific interest and speculation concerning the present objectives of the Council. Questions which have been raised in connection with the present method of operation have emphasized the need for further clarification of the Council's continuing activity in this field. Indeed the basic concepts which underlie the revised method of operation have not yet been fully appreciated by many of those familiar with the Council's former procedure. Thus, I welcome this further opportunity to present the fundamental objectives and significant aspects of the drug evaluation program of the A.M.A. Council on Pharmacy and Chemistry.

Inspection of Product Labeling and Literature Discontinued

Many of you will recall that the Council's former procedure embodied the consideration of commercial brands and formulations of drugs

Dr. H. D. Kautz discusses the A.M.A.'s new drug evaluation program at the ASHP Annual Meeting, held in Detroit.

which involved compliance on the part of manufacturers or distributors with certain rules, as a basis for their acceptance and inclusion in *N.N.R.* The former method of operation embraced not only the evaluation of evidence for new drugs, but also the repetitious process of examining labeling and product literature for marketed brands of the same drug. Accordingly, a large proportion of the time of the Council and its headquarters staff was occupied in the tedious inspection of product labeling and literature to determine its compliance with the former requirements for N.N.R. listing of commercially available dosage forms and sizes of drugs. However, in recent years, this activity gradually became superseded to a large extent by the increased regulatory functions of legal agencies: The Food and Drug Administration which implements the Federal Food, Drug and Cosmetic Act of 1938 and amendments of this law; the Biologics Control branch of the National Institutes of Health which administers the licensing of serums, vaccines and analogous products under the Public Health Service act of 1944. More significant than changing laws and related functions of the federal regulatory agencies, were certain trends and attitudes concerning drugs which had evolved during recent years and which gradually had undermined the effectiveness of the Council's former procedure. They explain more than other influences, the factors which led to the institution of the current program.

Effects of Increased Number of New Drugs

The decade following World War II was characterized by a tremendous expansion in the drug field mostly as a result of new drug discoveries, but partly through the development of more efficient methods for laboratory screening of promising new compounds. Not only were new drugs being developed with greater rapidity, but the number of available drugs was vastly increased. In earlier times hardly more than two or three new compounds a year were introduced for clinical use, whereas it is not now unusual for that number of new drugs to appear on the market within a single month. Some new compounds are near relatives of contemporary or older drugs and often are introduced merely to meet competition between manufacturers. Nonetheless they represent different chemical or biologic entities with slightly differing properties, and have swelled the over-all number of available therapeutic agents.

With the increased pace of new drug development there came also a corresponding expansion in the number of manufactured formulations and dosage sizes of drugs which in former days mostly were extemporaneously compounded by the individual pharmacist. This trend has extended to the introduction of all sorts of pharmaceutic specialities such as flavored preparations designed for pediatric use. Indeed, manufacturers have become so sentitive to the prescribing wants of physicians and the desires of patients, that all manner of ready-made formulations of drugs are reaching the market at an ever increasing rate.

The tremendous increase in the number of drugs and formulations has come about not only through modernization and expansion of existing manufacturing facilities, but also through the creation of new production and sales outlets. The competitive influence of industrial expansion has accounted for the multiplication of available brands of a given drug, as well as the development of additional competing similar-acting drugs. The variety of available antihistamine compounds is a striking example of the competitive multiplication of related drugs.

Appearance of More Highly Potent Drugs

Another trend of significance associated with the more rapid development of new drugs has been the introduction in recent years, of an increasing number of highly potent drugs, some of which exhibit narrow margins of safety between therapeutic and toxic dose levels. In the use of orally administered modern drugs, physicians no longer can rely on simple prescribing directions such as "one tablet t.i.d." that applied to many older oral drugs. This arises not so much from the fact that new drugs are available in a greater variety of manufactured tablet sizes, as from their increased potency which requires more careful

adjustment of the amount and interval of dosage to avoid untoward reactions.

The development of more potent agents for the control of disease and the expanded over-all number of available drugs, has been paralleled by a greater demand for more specific information in this field. With highly potent agents, more precise knowledge has become essential to their proper use. This also has stimulated greater awareness of the need for initial caution in the use of all new drugs, until sufficient clinical experience has been gained to gauge their long term untoward effects. Premature and over enthusiastic publicity in the lay press, often before reports can be found in scientific publications, has accentuated further the demand for current unbiased information on new drugs. Early, reliable and more complete information on drugs is thus in much greater demand than in former years.

Effect of Product Duplication

In the face of trends in drug development and the publicity which commonly precedes the marketing of new drugs, the Council found its former procedure inadequate to meet the expanded demands for information, chiefly because of the reduplication of effort involved in the examination of a greatly multiplied number of brands and formulations of each drug. It became apparent that this activity was hampering the freedom of the Council to provide current information on all basically new compounds and that a more efficient method of operation was needed to deal with modern methods of drug development.

It will be obvious from what has been said, that the current program of operation for evaluation of drugs has been remodeled along more flexible lines, and at the same time stream-lined to provide more timely information on all commercially available new compounds. The revised program not only eliminates certain disadvantages which hampered the attainment of this objective under the former procedure, but includes an expansion of the procedure by which the available evidence on new drugs can be reviewed by more experts in the field. Some of the significant features of the current program already are apparent; others, more obscure, require more detailed explanation.

New Evaluation Procedure

As redefined, the Council's drug evaluation function is to examine and evaluate available evidence relating to the actions, uses, dosage, hazards, and other pertinent properties of drugs and to encourage rational therapy by timely informative reports to the medical profession. The N.N.R. section of the Council's column of *The Journal of the American Medical Association* and annual editions of the book continue to serve as the Council's regular medium for the publication and dissemination of information on drugs. The scope of the book remains confined to descriptions of medicinal agents intended for use in or on the human body for the diagnosis, prevention or treatment of disease, and which are generally available in the United States. Ready-made mixtures combining two or more drugs, no longer are evaluated or described in *N.N.R.* because consideration of the enormous potential variety of such combinations would interfere with the Council's primary function to evaluate individual drugs. As in formers years, the current program provides for publication of Council reports on broader aspects of therapeutics which also appear in the Council's column of *The Journal,* but which are not intended for incorporation into *N.N.R.* Statements on individual drugs, as well as Council reports, also are individually reprinted as formerly, for distribution to meet separate requests for such information.

The chief alteration in the Council's N.N.R. column of *The Journal* and in the book consists in the elimination of the listing of commercial dosage forms and package sizes of drugs. This has been replaced in the Council's column by supplemental statements concerning the evaluation of additional uses and routes of administration, or re-evaluation of the status of previously evaluated drugs. Such statements serve as notices of significant revisions in N.N.R. monographs for succeeding editions of the book, and make the Council's column more newsworthy to physicians as a source of current therapeutic information.

Trade Names

Under the present program provision has been made for indicating trade names in conjunction with nonproprietary terminology under which all evaluated drugs are described. Such names are included as a matter of information for those unfamiliar with nonproprietary names for drugs, but are limited to names which are applied to preparations intended for clinical uses evaluated by the Council. Identification of manufacturers, distributors or owners of trademarks, or the particular formulations and sizes of preparations to which they may be applied is no longer specified. This type of information has been excluded to eliminate the task of recording and revising such details and to discourage the use of *N.N.R.* as a book of "accepted" remedies. The Council thus leaves to the pharmacist and the detail man, the function of supplying physicians with product information on drugs.

Promotional Literature

While essential to the efficiency of the current method of operation, the elimination of the examination of drug labeling and product literature issued by pharmaceutical firms has a further significance. The Council's previous attempt to discourage unwarranted claims through supervision of pharmaceutical literature for physicians failed to achieve this on a sufficiently wide scale because of unwillingness on the part of some manufacturers to comply with suggested revisions. Despite the excellent performance of many drug firms in providing reliable information concerning new drugs, physicians should be aware of the temptation in this highly competitive field to circularize promotional literature which emphasizes favorable and minimizes unfavorable facts relating to their usefulness. The Council's withdrawal from the consideration of such material may encourage more physicians to seek information on new drugs in the Council's column of *The Journal* and in *N.N.R.* Unless pharmaceutical manufacturers assume greater responsibility for presenting both the disadvantageous and advantageous features of new drugs, promotional literature will be viewed with ever increasing skepticism by the medical profession.

Greater Freedom of Council

Probably the single most significant feature of the current program is the greater freedom of the Council not only to evaluate all available drugs, but to publish statements concerning them for inclusion in *N.N.R.* whether or not the existing evidence is adequate to warrant favorable conclusions. It is believed that publication of fair comment and criticism in monographs and statements on drugs which are marketed without adequate supporting evidence or are promoted with extravagant claims, will attract the attention of more physicians and exert more influence upon manufacturers than the former acceptance procedure. Of even more scientific importance, is the possibility that the revised program ultimately may influence manufacturers to obtain more conclusive evidence to support the use of new drugs before they are placed on the market.

Another feature of the Council's revised program involves the expansion of its method of evaluating new evidence on drugs. As noted earlier in this presentation, wider sampling of the opinions of outside experts as consultants is obtained regarding the available evidence pertaining to all fundamentally new drugs or new uses of older drugs. This provides a wide range of the views of experienced clinicians respecting the proposed use, administration and dosage of drugs from which the Council can make a fair appraisal of the available scientific data.

It can be concluded that institution of the current program has created a much freer atmosphere in which the Council on the one hand and industry on the other, can achieve their individual purposes. It is hoped this climate not only will preserve, but also enhance, the cooperative attitude which industry has shown in the past toward the function of the Council as a scientific drug-evaluating body. Under the current program, manufacturers have demonstrated their willingness to submit scientific data for evaluation of new drugs and new uses of drugs. The Council continues to invite manufacturers to forward copies of all available laboratory and clinical reports of investigations (published and unpublished) for evaluation of individual drugs and their uses. Manufacturers now are free to do this without submitting product labeling or literature for review by the Council. Cooperating manufacturers also are given the privilege of commenting on N.N.R. monograph and supplemental statements prior to publication by the Council and also receive credit for supplying scientific data as each statement appears in the Council's column of *The Journal of the American Medical Association.* With this procedure both the Council and pharmaceutical outlets benefit from the exchange of views concerning the validity of evidence to support new drugs and new uses of drugs.

Selection of Nonproprietary Names

The Council continues to encourage manufacturers to cooperate in the selection of suitable convenient nonproprietary names for new drugs under which they can be described in the Council's column of *The Journal* and in *N.N.R.* Such terminology also is desirable for use in other scientific publications and promotes universal interest through the application of uniform nomenclature. The Council wishes to be informed of domestic trade names for drugs so that this information also can be included as it applies to drugs evaluated and described in *N.N.R.* The Council believes listing of trade names is desirable to stimulate readership by a maximum number of physicians and thus increase the dissemination of unbiased information on drugs.

It is the hope of the Council that the current drug evaluation program is providing a better service to the medical profession. Physicians and others concerned with the drug field are urged to read the Council's column in *The Journal of the American Medical Association,* and to consult *New and Nonofficial Remedies* for unbiased information on all new drugs, as the Council is able under its revised procedure, to provide more complete coverage of this important subject.

MANAGING THE AFFAIRS OF THE PHARMACY COMMITTEE

by JOSEPH P. CRISALLI

ORDWAY TEAD IN HIS BOOK "The Art of Administration" talks of Democratic Administration as being concerned with getting a job done economically and expeditiously in terms of the attitudes and efforts of the participants. Democratic administration assures concurrences in the aims, working policies, and methods of those who are eager to contribute their best creative efforts towards the realization of an organizational objective. The committee process is one of administration's methods of utilizing and stimulating group thinking. The result is a pooling of knowl-

JOSEPH P. CRISALLI is Chief, Pharmacy Branch U. S. Public Health Service Hospital, New Orleans, La.

edge and experience to cope with organizational problems that cut across departmental lines, which cannot be handled independently or by edict but must be solved by cooperative effort. This is the nature of the Pharmacy Committee; its objective being to mold adjacent viewpoints into an integrated agreement and committing those who participate in this to join in seeing it through.

History of Pharmacy Committee

In hospital circles the need for a coordinating force affecting pharmacy activities was recognized in the early '20's. It was then that the problem of duplication was beginning to show its effects. Edward Spease early advocated the establishment of therapeutic or pharmacy committees consisting of members of the medical staff, with a pharmacist as secretary, to deal with matters of a pharmaceutical nature which touched upon the affairs of other departments and ultimately affected patient welfare. The idea was to get the best pharmaceuticals for the investment made and to pass this benefit on to the patient. The principle of the pharmacy committee was later incorporated into the Minimum Standard for Pharmacies as adopted by the American Society of Hospital Pharmacists and approved by the American Pharmaceutical Association and the American Hospital Association.

Functions of Pharmacy Committee

In its broadest sense the function of the Pharmacy Committee is one of coordination. Through the Pharmacy Committee, the hospital staff obtains an advised selection of drugs which constitutes the best thinking in the hospital. In this way the maximum is derived from the money spent for drugs, and the patient benefits from the selection. Over the years we have learned to identify and enumerate the areas where this coordination is most effective. Thus the purpose of the pharmacy committee has been variously stated as being:

1. To develop a formulary of accepted drugs
2. To evaluate clinical data concerning drugs
3. To review the drug stock situation to prevent disuse and minimize obsolescence
4. To serve as an advisory group to the pharmacist concerning the choice of drugs to be stocked

Because hospital organization is composed of highly specialized departments, the coordinating influence of the Pharmacy Committee is essential within its allotted area. Within this group, the representatives of the departments concerned meet to discuss and accept an integrated solution to their problems. Unilateral action is unthinkable for it would mean useless multiplicity and duplication of drugs and in another respect, uncoordinated activity.

Towards Greater Effectiveness

Yet to have a committee is little short of none at all, if it is defective. How many of us have thought our meetings uninteresting, nonproductive, and not worthwhile at one time or another? How many of us have seen our decisions fade into oblivion through lack of sustaining action? The effectiveness of our committee can only be measured in terms of good members, good meetings, and good follow-up. This is the substance of our paper.

The Members

The Pharmacy Committee can only be as good as those who compose it. The criteria to consider in choosing members from the professional staff must be their knowledge of the problems encountered and their ability to think and work with others in pursuing committee aims. Largely because Pharmacy Committee affairs affect the conduct of the pharmacy's business, the pharmacist is vitally concerned about the attitudes and capabilities of prospective members. As permanent secretary of the Pharmacy Committee, the pharmacist is in excellent position to give advice on the choice of members. It is recognized that organizational decorum may strongly influence member selection. To a large degree membership is reserved to the heads of departments. Whether selection is governed by organizational set-up, or whether choice is entirely free, a certain amount of indoctrination is always necessary. This constitutes an equalizing force for if we are deprived of free choice, the alternative is more indoctrination.

But our concern here is not with choice but with capacity for good membership. Each member must first of all show interest. This comes naturally to him if he is to represent his department effectively at the meetings of the committee. Each member must feel himself a part of the group, be willing to express himself freely, and be motivated by a desire to join in working out a solution that is acceptable to all. In the Pharmacy Committee there is no room for the self-centered nor for one who tries to turn everything into a personal victory. The good member will familiarize himself beforehand with the subject to be discussed, so as to contribute substantially to the discussion. He will participate actively in an analysis of the problem, listen attentively to what is said, and remain totally objective throughout. Bickering, arguing, arrogance, or hostility have no place at a meeting. The dominator, the blocker, and the hibernator who revive in time to second the motion to adjourn are disconcerting and cause a general loss of interest.

In short, the good pharmacy committee member must have a knowledge of the matter under discussion, a quick mind to follow closely, sound judgment for a good decision, and good speech to convey his thoughts. His attitude toward the group is important; he must be sympathetic toward the aims of the pharmacy committee to be of value to it.

Customarily the Clinical Director or the Chief of Medicine is Chairman of the Pharmacy Committee. Here again courtesy has played a major part. I do not feel that the chairmanship of the pharmacy committee should be tied exclusively to one of these two offices. To repeatedly appoint one or the other to the chairmanship may appear to some as the application of subtle form of pressure. Further, it tends to identify the chairmanship with these positions. The important think to consider in appointing a chairman is his understanding of the pharmacy committe and its problems, and his ability to conduct a discussion to a successful conclusion. The chairmanship in the pharmacy committee is more responsibility rather than privilege. In informal discussion leadership shifts from person to person depending on who is contributing to the discussion for the moment. The chairman has a dual role to perform, that of *participant* on equal terms with other members, and that of appointed chairman when there is need for guidance. Indeed, depending on the proficiency of the members of the committee, he is probably more often participant than chairman.

Aside from a knowledge of the subject, the chairman must be a discerning thinker able to confront the unexpected in a rapid changing situation. He should be able to listen attentively, weigh viewpoints, respect opinions, and possess a moderate sense of humor to promote equanimity and to support favorable attitudes throughout the discussion. Finally, he must be willing to plan in advance of the actual meeting, analyzing and defining the scope of the problems to be discussed, because then he will be better equipped to give the guidance that is required of him.

As has been mentioned before, the pharmacist is the committee's secretary. This is the ideal spot for him because it puts him close to the chairman and makes him part observer and part-time participant. The pharmacist must be able to accumulate data which is later incorporated into an agenda for discussion. He must have the ability to ferret out problem areas, to bring these to the chairman and then to talk about them intelligently to the committee, whether he is asked to present them or if he is queried concerning them. In the committee room he is somewhat beside the others. Since the pharmacy committee is advisory to the pharmacist, his role may involve persuasion and defense as well as participation in the contributory manner of the other members. His work before the meeting and afterwards must be meticulous if the most is to be derived from committee efforts. During the meeting he must be attentive and observant so that he can advise the others in the light of his experience in order to prevent the making of regrettable decisions that may have to be reserved. Aside from this, he must be able to work with the group carrying out their recommendations whether they please him or not.

The Meeting

There are a number of arrangements to be made prior to a meeting. The physical setting should be conducive to relaxed thought and the hour should be chosen for the convenience of the members. It is best to meet when everyone is likely to be free from pressures for then they will be at ease. Care must be taken to have at hand all mechanical aids, charts, etc., needed to exploit the subject adequately. Notice of the meeting should be forwarded to the members well in advance of the appointed day.

While an opportunity should be afforded for members to introduce new subjects from the floor, it is necessary to prepare an agenda. This will ensure full coverage and govern the course of the meeting. If this is not done, sidetracking and irrelevant talk will creep into the discussion with the result that far less is accomplished than was expected. The agenda gives direction to the discussion, saves invaluable time, and hastens a decision. At the same time, some deviation should be allowed if properly monitored for the purpose of exciting casual interest among the members. The agenda is usually the work of the chairman and the secretary. Items of committee interest come to the attention of the pharmacist through daily contacts with other departments of the hospital. Other members suggest other items that they would like included in the agenda. These are weighed, sifted, and consolidated into the outline called the agenda, in a conference between the chairman and secretary. The nature of the agenda should be such as to invite discussion. Its manner should be predominately interrogative. It should include a statement of the problem, the facts involved, possible alternative solutions, and methods of effectuating the most plausible solution. These are offered suggestively to the members through the agenda to stimulate thought and prepare them for intelligent discussion. The agenda must be presented to the members far enough in advance of the meeting to enable them to formulate opinions.

The meeting opens with at least two well informed members—the chairman and the secretary.

They have labored to produce a methodical meeting setting the stage for free but determinate discussion. They are familiar with the attitudes and inclinations of most of the members through previous contacts and can anticipate the probable course of the discussion. This of course will aid the chairman in meeting objections by making him more discerning. The chairman's job is particularly exacting as he strives to integrate the viewpoints of departmental specialists whose opinions are slanted by their professional leanings. In the face of these inclinations, the chairman must be a guide, a stimulator, and coordinator with a good sense of timing. He must know what to do and when to do it. If he is to have a successful meeting, if he is to make it productive, if he is to invite integrated action he must be thoroughly prepared to meet each situation as it arises. His job is somewhat lightened by a sense of shared responsibility felt naturally by the members. They have assembled to reach agreement. The chairman must promote conditions that favor successful discussions and conclusions. He must meet adverse comment with adroit remark. There are times when prudence will dictate postponing a decision, or dropping a controversial question to a more favorable moment. The wise chairman will wait. There are times when pressing for a vote will check the trend towards unanimity. This is undesirable. Finally, there is the time when he must urge caution to prevent the onrush towards an ill-conceived solution which may complicate further a fairly complex situation.

Someone has said that group deliberation aims at cooperative solution through reflective thinking. The best results can only be achieved if the members are ready to take an active part in the process. From the agenda they learn in advance what the meeting will entail and will do some thinking about the topics. The meeting is opened by the chairman who states the facts and asks a leading question. Someone will answer. To be effective, participation must involve all the members; it must be broad; it must be contributive. If there is reticence in one or more member; if the exchange is largely a private affair between two members, the chairman should try to draw the others into the discussion by referring questions to them and affording them every opportunity to speak. Particularly talkative individuals may be halted at the first opportunity by commenting on the fine quality of their contribution, at the same time asking for comment from one of the other committeemen. Problem members in general must be handled, with forethought, politely but firmly. It is the chairman's duty to quickly put an end to all irrelevant discourse, heated arguments and personal attacks. This must be done at the first indications of such conduct. A humorous remark by the chairman and reverting back to course, at the same time maintaining objectivity, will avert strained feelings. The member, on his part must remain conscious of the need for well ordered group thinking, must have a sense of direction and be willing to stay on the track. He should be receptive, openminded and cooperative, able to see the present in terms of the future. He will recognize the effects of committee labors on activities of the future and will be satisfied only when all pertinent factors have been completely thrashed out.

In short, the responsible committee member is able to ask discerning questions because he has previously prepared himself for the discussion; will maintain equanimity for orderliness and will engage in constructive forward-going participation in the interest of thoroughness. The chairman repeatedly attempts to crystallize thinking by identifying alternatives, by constantly summarizing to associate dangling areas of agreement or disagreement and by recapitulating at the close to firmly establish what has been accomplished.

The Follow-up

During the meeting the pharmacist-secretary acts in two capacities: as a source of information and as participant. His position is rather complex. He is informed on matters relating to drug usage in a broad way as distinguished from the specialized knowledge of most of the other members. He is informed in a special way on pharmaceutical matters pertaining to his department. He is therefore both a generalist and specialist, adviser and participant at the meeting. A foolish notion is the picture of the pharmacist-secretary taking down minutes of the meeting and trying to follow the discussion at the same time. The recording of minutes is not the job of the secretary. Clerical help should be made available. Taking notes is greatly simplified if a careful agenda has been prepared. The barest notes alongside the items on the agenda will bring to mind much of what occurred during the meeting and will supply the information needed for coherence. This method will free the secretary for more active participation in the event a stenographer is not available.

Because the pharmacist is broadly informed on committee matters, by virtue of his office as secretary, he is called upon frequently by the chairman to furnish pertinent material. He becomes the subject of much of the questioning from the members who desire clarification. It is here that adequate preparation becomes important. After all the facts are out he becomes a participant agree-

ing, interjecting or disagreeing like the others, until a solution is reached.

Yet the work of the secretary has only begun at the end of the meeting. The steps necessary to translate recommendations into policy must be taken. The minutes of the meeting have to be written, approved, and forwarded to the members. After approval by the administrator a memorandum must be issued to all departments and staff members who will be affected by the new policy. Later, follow-up will become necessary because people tend to lapse back into old habits. At the same time, the pharmacist-secretary is accumulating new material for discussion at the next meeting. As if this were not enough, dissatisfaction often arises out of decision made. This cannot be ignored, grumblings must be traced to their sources, tension must be erased and unfavorable attitudes must be modified. The pharmacist must be able to discuss the situation on a private basis intelligently and diplomatically with the critical individuals. This responsibility of course, is shared with the other members of the pharmacy committee, but by virtue of his position the burden largely falls on the pharmacist. From all of this, it becomes very apparent that success of committee undertakings depends largely on the diligence and persistence of the pharmacist and the way he carries on his work.

Summary and Conclusion

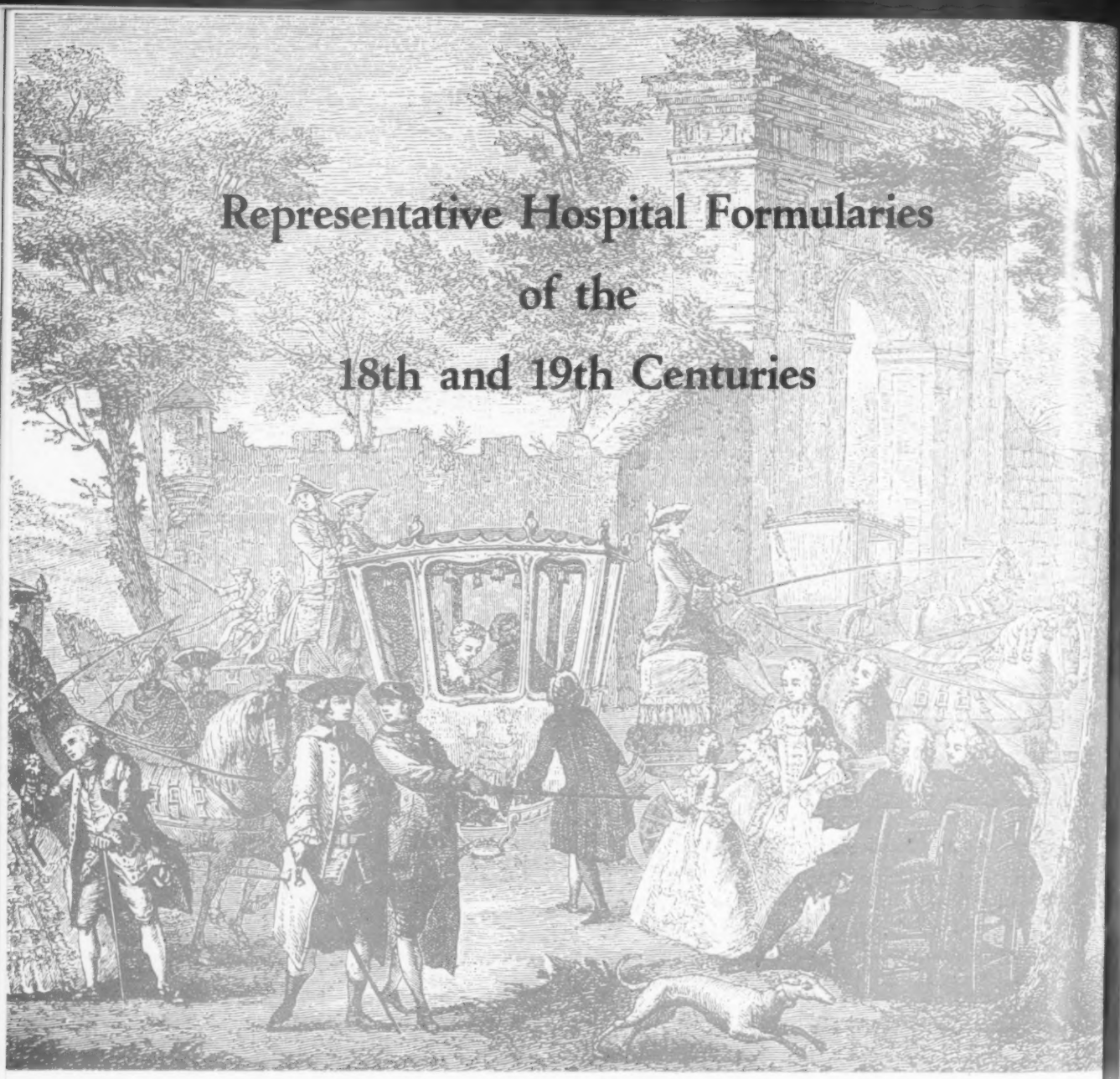
We have shown that the effectiveness of the pharmacy committee is dependent on its members, the interest they have in the committee, the leadership qualities of the chairman, and the persistent efforts of the pharmacist to communicate its approved recommendations to the staff. We have seen that preparation and participation are important for a satisfying meeting. The essentials necessary for a successful meeting may be stated as follows:

1. Making plans for the meeting
   a. defining the problem(s)
   b. presenting the facts, analyzing them
   c. determining the criteria for a good solution
   d. examining plausible solutions
   e. tentative thinking in terms of action to be taken.
2. Preparing the agenda from the above using the interrogative sentence to stimulate thought.
3. Preparing for the meeting
   a. notice of meeting
   b. distribution of agenda
   c. comfortable meeting place
   d. mechanical aids.
4. The meeting itself
   a. starts and ends on time
   b. members stick to agenda; full discussion of vital points
   c. members actively participate
   d. chairman keeps meeting moving in right direction
5. Minutes are written immediately after meeting.
6. Staff is informed of committee actions as soon as possible after administrative approval.
7. Certain problems are encountered at a meeting. They are generally the responsibility of the chairman:
   1. Poor participation (stimulation)
   2. Lack of focus (better planning necessary)
   3. Overdiscussion (recognize when discussion is no longer productive)
   4. Lack of progress (leading questions)
   5. Negative member characteristics (dominator, blocker, cynic, etc., use courtesy, restraint tactics, firmness)
   6. Personality centered discussions (termination, humor, changeover).

To me the pharmacy committee represents an opportunity for professional growth. Seated around the conference table with his confreres, the pharmacist has emerged from his department and has been accepted as a full partner on the hospital team. This has not come about easily. Prejudices had to be broken down; the idea of intrusion by the pharmacist had to be dispelled; the pharmacist himself had to learn that he was not a second-rater and that he had something worthwhile to contribute, but mostly that he had to get out and plug for what he wanted.

Those of us who do not have a pharmacy committee need only to be reminded that it will help them run their department more smoothly and in consonance with the rest of the hospital team. Much friction, irritation and backwash can be eliminated by discussion around the committee table. The pharmacy committee is a team approach to problem solving. Management has long recognized its benefits. Your administrator will be quick to note its advantages. The rest of the hospital will be gratified with the results. The pharmacist will enhance his prestige.

When you have convinced yourself that a pharmacy committee has a place at your hospital, you should approach the administrator but not before you are thoroughly prepared to answer all of his questions. If done properly there is no doubt but that the administrator will support the idea. A common error is to become discouraged at the first trial. Keep working at it; gather facts about successful committees from publications and present these to him. After he is receptive to the idea, visit the Chiefs of Services. The job of selling the pharmacy committee to some may not be easy, but if your preparation is thorough and if you persist in your efforts without appearing as a nuisance, you will realize your objective. Beyond this point it is all nip and tuck—just follow the common sense rules of committee procedure.



Representative Hospital Formularies of the 18th and 19th Centuries

by ALEX BERMAN

Evolution of the Printed Hospital Formulary

THERE IS EVIDENCE that the printed hospital formulary is more than three hundred years old.* Both von Scherer and Fritz Ferchl indicate that the hospital of the city of Messina, Sicily, possessed a printed formulary as early as 1642.[1] In 1619, the famous German physician, Raymund Minderer (1570-1621) published a manual of military medicine which contained a list of easily prepared medicines (*"ac facile parabilia medicamenta continens"*) for use in military exigencies.[2] Whether Minderer's work can be regarded as a true military hospital formulary is debatable. Leclaire categorically states that the first book of formulas to be printed for the use of military hospitals in Europe was published for the French army by royal edict in 1747.[3]

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* Manuscript hospital formularies were compiled in medieval hospitals. Jean Volckringer has mentioned their presence in French archival collections. (See Volckringer, J: *Evolution et Unification des Formulaires et des Pharmacopées,* Paris, 1953, p. 22).

By the end of the seventeenth century, the Hôtel-Dieu of Lyons could boast of a volume compiled by Pierre Garnier which listed in Latin and French the "new formulas" for medicines used at that institution.[4] During the second half of the eighteenth century, the European hospital formulary became increasingly commonplace and in London, the production of hospital formularies was clearly linked with the English voluntary hospital movement of that century.[5] The first decades of the nineteenth century saw the rise of Paris as the medical and hospital center of the world, thus providing an excellent milieu for the further growth of hospital formularies. This period was ripe for the appearance of the outstanding work of Parmentier, Ratier, Foy, Milne-Edwards and Vavasseur.[6] By the end of the eighteenth century, virtually every major European country had its hospital formularies.[7] In this country, two military hospital formularies were printed during the throes of the Revolutionary War—the famous *Lititz Pharmacopoeia* (1778) and Coste's *Compendium Pharmaceuticum* (1780).[8]

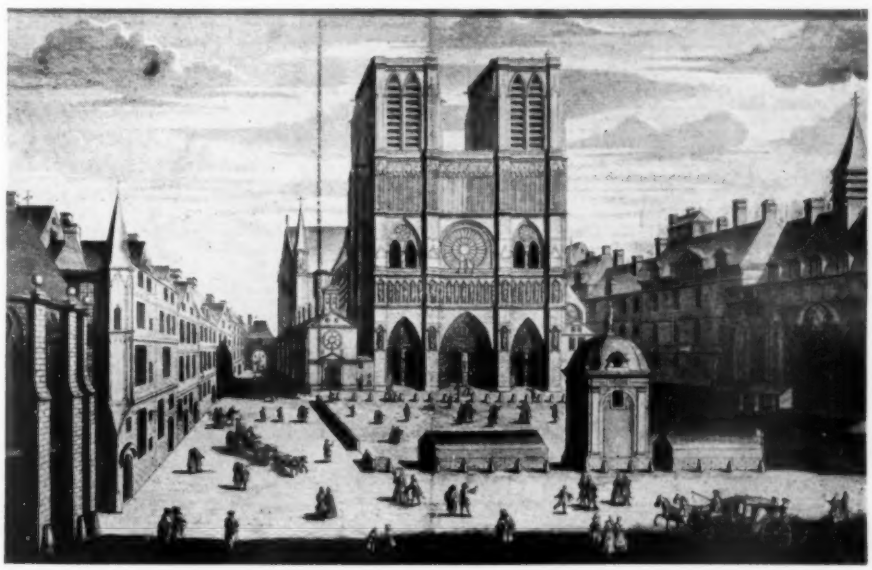
The span of 186 years intervening between the appearance of Garnier's *Nouvelles Formules* in 1693 and the issuance of Balmanno Squire's *Pharmacopoeia of the British Hospital for Diseases of the Skin* in 1879 saw the production of a remarkable diversity in types of formularies. Not only were there formularies for general hospitals, but also for specialized ones (skin, throat, etc.);[9] for army installations,[10] naval hospitals,[11] and combinations of both.[12] Moreover, there were compiled hospital formularies which were collections of prescriptions used in hospitals of individual cities,[13] and at least two "global" hospital formularies were written in this period.[14]

Hospital Therapeutics Mirrored

Three hundred years of hospital therapeutics are mirrored in the development of the printed formulary. We have come a long way, therapeutically speaking, from the "Pleuretick Infusion" listed in Banyer's *Hospital Dispensatory* of 1718 which had as one of its ingredients six ounces of "fresh Horse-dung."[15] To be sure, the author was conscious of the potency of this remedy, for the reader was told that "If the dose here mentioned be too noisome, it may be lessened, and repeated the oftner." The quaint admonition of another eighteenth century English formulary that "Patients upon Low Diet, shall have one Loaf of Bread per Day. One Quart of Beer per Day, from Lady-day to Michaelmas. One Pint per Day, from Michaelmas to Lady-day,"[16] sounds strange to readers of modern hospital formularies used to involved chemical nomenclature and structural formulae.

The hospital formulary is no longer the monopoly of the physician; responsibility for compiling formularies has now shifted to Chief Pharmacists working as Secretaries of Hospital Pharmacy and Therapeutics Committees. But this shift has come relatively recently—especially in this country. With few early exceptions, notably in France,[17] hospital pharmacists have until comparatively late times been divorced from this important task.

The modern hospital pharmacist is as far removed from his monastic forbear as today's hospital is from the medieval *nosocomium*. A complex of forces—social, educational, technological, scientific—have through the centuries shaped the practice of pharmacy within the hospital. The hospital formulary has not escaped this impact, as the subsequent survey will show.



A 17th-century illustration of the Hôtel-Dieu in the foreground left. The cathedral of Notre Dame towers in the center.

From Fosseyeux's **L'Hôtel-Dieu de Paris au XVII^e^ et XVIII^e^ Siècle.**

1. Pisani, Petr. Paul: *Antidotarium speciale hospitalis nobilis urbis Messanae.* Messina, 1642. Cited by Fritz Ferchl: *Chemisch-Pharmazeutisches Bio - und Bibliographikon,* Mittenwald, 1938, p. 414, and by A.N. von Scherer: *Codex Medicamentarius Europaeus,* Sectio Septima, Leipzig, 1822, p. 147.

2. Minderer, Raymund: *Medicina militaris s. libellus castrensis euporista ac facile parabilia medicamenta continens,* 1619. Other editions appeared in 1621, 1623, 1634, 1640, 1660 and 1672. An English edition was published in 1634. A German edition was also brought out. Minderer's work was undoubtedly used by the German military barber-surgeons (*Feldscherer*).

3. *Formules de pharmacie pour les hôpitaux militaires du roi. . .* Paris, 1747. Cited in *Revue d'Histoire de la Pharmacie, 3*:192, 1932.

4. Garnier, Pierre: *Nouvelles formules de médecine, latines et franc. pour le grand Hôtel-Dieu de Lion . . .* Lion, 1693, and several later editions.

5. For a history of the voluntary hospital movement in England, see A.D. Evans and L.G. Redmond-Howard: *The Romance of the British Voluntary Hospital Movement,* Hutchinson & Co., London, n.d.

6. Parmentier, J.A.A.: *Code pharmaceutique à l'usage des hospices civils des secours à domicile et des infirmeries des maisons d'arrêt,* Paris, 1803 and later editions; Ratier, F.S.: *Formulaire pratique des hôpitaux civils de Paris,* Paris, 1823 and several later editions including translation into English; Milne-Edwards, H., and Vavasseur, P.: *Nouveau formulaire pratique des hôpitaux ou Choix de formules des hôpitaux civiles et militaires de France, d'Angleterre, d'Allemagne, d'Italie,* etc., Paris, 1832; Foy. F.: *Nouveau formulaire des praticiens . . .* Paris, 1833.

7. See von Scherer, *op. cit.,* pp. 135-162.

8. These two formularies have been exhaustively discussed in the following works: Kremers, E.: *Documents pertaining to the Medicinal Supplies within the North American Colonies from 1643 to 1780.* (Introduction and supplement by Dr. George Urdang) Madison, Wisconsin, 1944; Kremers, E., and Urdang, G.: *History of Pharmacy,* 2nd ed., Philadelphia, 1951.

9. For example, Mackenzie, M.: *The Pharmacopoeia of the Hospital for Diseases of the Throat,* Lond., 1872, and B. Squire's work already mentioned.

10. Army formularies during this period are too numerous to be listed.

11. For example, *Formules pharmaceutiques . . . des remèdes . . . dans l'hôpital royal de la marine de Brest,* Brest, 1769; *Pharmacopoea navalis Rossica,* Petrograd, 1783 and 1784.

12. For example, *Pharmacopoeia militaris, navalis et eorum usui accomodata, qui inpensis publicis curantur.* Holmiae 1789 [Sweden]

13. Such compilations as that of Ratier cited above, and the formularies of Henry Banyer: *Pharmacopoeia Pauperum: or the Hospital Dispensatory Containing the Medicines Used in the Hospitals of London,* 1718 and later editions.

14. The formularies of Milne-Edwards and Vavasseur and that of François Foy cited above.

15. Banyer, Henry: *Op. Cit.,* p. 58.

16. *The Modern Practice of the London Hospitals,* London, 1764, p. iv.

17. Claude-Joseph Geoffroy (1685-1752), co-author of the first French military formulary in 1747; Parmentier, and Foy.

The first published formulary of the

Hotel-Dieu Of Paris

FORMULES MEDICINALES DE L'HOTEL-DIEU DE PARIS, . . . PARIS, 1753

IT WOULD BE AN UNDERSTATEMENT to say that the large European hospitals of the eighteenth century were unfit to house sick people. Not until the devastating exposé of J.R. Tenon (*Mémoires sur les hôpitaux de Paris,* Paris, 1788) and the appearance of John Howard's detailed description of the appalling conditions in European prisons and hospitals (*The State of the Prisons in England and Wales,* Warrington, 1777 and *An Account of the Principal Lazarettos in Europe,* Warrington 1789), did serious attention focus on necessary reforms.

Standing on the bank of the Seine, in the shadow of the Cathedral of Nôtre-Dame, the Hôtel-Dieu of Paris in the eighteenth century ministered to thousands of patients annually. Most of its approximately 1200 beds harbored from four to six people. In the absence of proper ventilation, hygiene, and segregation of contagious cases, mortality rates were exceedingly high.

Although Maurice Bouvet has shown the existence of manuscript formularies of the Hôtel-Dieu dating back to 1720 or 1730, and has also indicated that certain of the medical recipes used at that institution were published as part of general medical works[1], it was not until 1753 that the first distinct and separate edition of the Hôtel-Dieu formulary was printed.

This pocket-sized book of 216 pages was compiled by a mysterious Monsieur M., whose identity is completely obscure. On page 5, however, we are informed that this work had been decisively influenced by Col de Villars (1675-1747) who had served as a physician at the Hôtel-Dieu and had been Professor of Surgery on the Faculty of Medicine.

A long essay of twenty-eight pages entitled "On the Utility which results from employing the

1. In J. Allen's *L'abrégé de toute la médicine pratique (1728) and Supplément de l'abrégé de toute la médicine pratique par . . . Docteur en Médicine,* (1741). Cited by M. Bouvet in *La Pharmacie Française, 38*:9-15, (Sept.) 1934.

FORMULES
MEDICINALES
DE
L'HOSTEL-DIEU DE PARIS,
OU
PHARMACOPÉE,
Contenant la compoſition & la doſe des Remédes les plus uſités.
Par M. M*** Docteur en Médecine de la Faculté de Montpellier, & Aggrégé en l'Univerſité d'Aix.
A PARIS, RUE S. JACQUES,
Chez {DESPILLY, Fils, Libraire, à la Vieille Poſte. / J. CH. CHARDON, Fils, à la Couronne d'Or, près la Fontaine S. Severin.
M. DCC. LIII.
Avec Approbation & Privilege du Roi.

French language in the sciences, above all in medicine," preceded the presentation of the remedies used at the institution. Numerous reasons were advanced by the author for favoring French over Latin for scientific purposes; one important reason given was that the chances of error would be minimized. However, the second enlarged edition which appeared in 1767[2], was written in both French and Latin and listed not only the formulas of the Hôtel-Dieu, but also those of two other hospitals - la Charité and l'Hôtel Royal des Invalides.[3]

Many types of pharmaceutical preparations are mentioned in the first edition[4], such as Tisanes, Infusions, Decoctions, Apozemes, Juleps, Potions, Syrups, Lohochs, Hydromels, Medicated Bouillons, Medicated Wines, Gargles, Powders, Boluses, Tablettes, Troches, Opiates, Collyria, Solutions for Enemas, Fomentations, Cataplasms, Liniments, Ointments, Emplasters, Bougies, and a few miscellaneous nostrums.

This work was clearly permeated with the polypharmacy and the bizarre therapeutic concepts of the time. Included in the materia medica of the book were such ingredients as powdered crab, vipers, and blood of a wild goat.[5] Also prominently featured in the formulary, and highly recommended for vesical calculus, was the famous nostrum concocted by Joanna Stephens, which the English Parliament had purchased for 5,000 pounds in 1739[6]. The formula, which had been published in the *London Gazette* of June 19, 1739, consisted of such items as calcined egg shells and snails, soap, and miscellaneous herbs.

2. Bouvet states that the second edition appeared in 1767. (*Op.cit.*, p. 15.) This is also the date given by E. H. Guitard: *Manuel d'Histoire de la Litterature Pharmaceutique*, Paris, 1942, p. 111. Marcel Fosseyeux, however, gives the time as 1762 in his *L'Hôtel-Dieu de Paris*, Paris, 1912, p. 322. Fosseyeux's date is accepted by Albert Goris in his *Centenaire de l'Internat en Pharmacie*, Paris, 1920, p. 73.

3. The title read *Formules de médicamens usitées dans les différans hôpitaux de la ville de Paris. Avec leurs vertus, leurs usages et leurs doses.* A third edition appeared in 1780, and a reprint in 1783. (Bouvet, *op.cit.*, p. 16.)

4. Nicolas Lemery (1645-1715) defines some of the terms in his *Pharmacopée Universelle*, 2nd edition, Paris, 1716. "Tisane" is defined as a weak decoction which is made as palatable as possible. An "Apozeme", on the other hand, is defined as a strong decoction or infusion of many ingredients. A "Julep" is stated to be a preparation of syrups mixed with distilled waters or decoctions. A "Lohoch", a term of Arabic derivation, was Latinized into "Linctus", and was a thick syrupy preparation that had to be licked. "Hydromels" were made by incorporating ingredients in honey and water; and "Tablettes" were defined as "solid electuaries".

5. Appears in the formula for *Potion Diaphorétique* on pp. 66-7, 1753 ed.

6. Appears on pages 163-175 of the 1753 edition.

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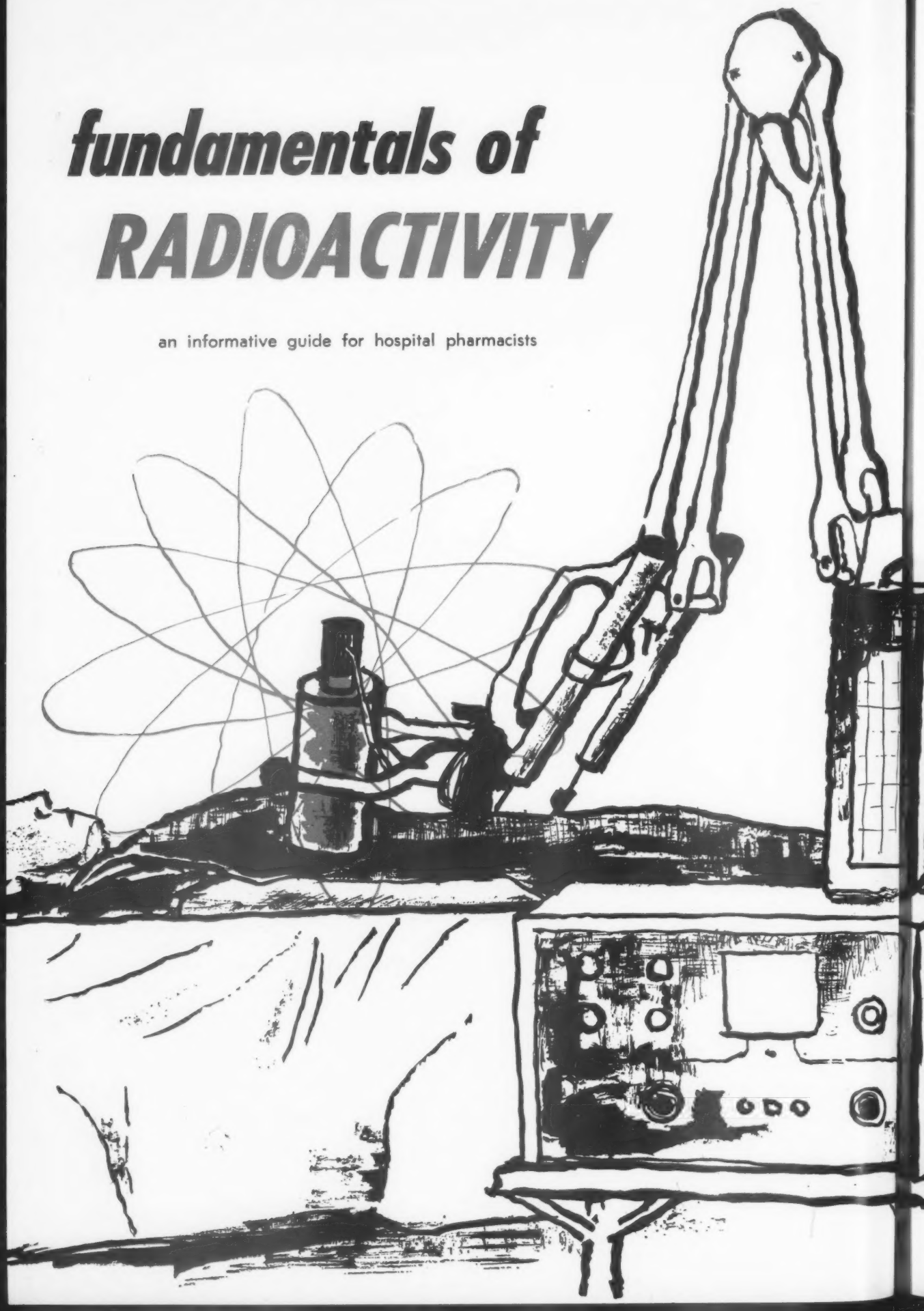
fundamentals of RADIOACTIVITY

an informative guide for hospital pharmacists



by CLIFTON J. LATIOLAIS

this guide provides the hospital pharmacist with fundamental information on radioactivity and provides the answers to these important questions:

What is radioactivity?

What are the characteristics of radiation?

How is radioactivity detected?

What are the hazards of radiation?

What are radioactive isotopes?

How are radioactive isotopes produced?

THE MEDICAL USE OF RADIOISOTOPES has increased to such proportions that radioactive drugs are now being used as frequently as many nonradioactive drugs. These radioactive pharmaceuticals are used primarily in the hospital. The hospital pharmacist, therefore, is challenged with the responsibility of handling and dispensing them.

To dispense radioactive isotopes for medical purposes a pharmacist needs to know some of the principles underlying radioactivity. It is not necessary that the pharmacist know all about nuclear physics to learn these principles.

The purpose of this paper is to present some aspects of radioactivity in terms understandable to the pharmacist. By showing that it is not necessary to have an extensive knowledge of nuclear physics, it can encourage hospital pharmacists to provide a radioactive pharmaceutical service.

RADIOACTIVITY

Discovery

For nearly 2000 years, scientists took for granted that the atoms of an element were as indestructible as Democritus had postulated. Democritus, a Greek philosopher of the fifth century B.C., gave the world its first concept of the atom. He was the first person to conclude that matter is composed of ultimate particles which are not capable of being subdivided.

Our knowledge of radioactivity dates from 1896 when Henri Becquerel performed an experiment which did away with the concept of the immutability of the atom. Becquerel noted that some uranium salts emitted an invisible radiation capable of penetrating thin layers of opaque material and affecting a photographic plate.

The knowledge gained through Becquerel's experiments led Pierre and Marie Curie in 1898 to conclude that uranium rays were an atomic phenomenon characteristic of the element and not related to the chemical or physical state. This phenomenon the Curies called "radioactivity."

Types of Radioactivity

Natural. All elements, with atomic number greater than 83 (Bismuth), found in natural sources are radioactive. These elements belong to one of three radioactive chains (series). These are:

(1) Uranium. The uranium series consists of uranium (mass 238) as the parent substance and radium G (lead with mass 206) as the stable end product. See Table 1.

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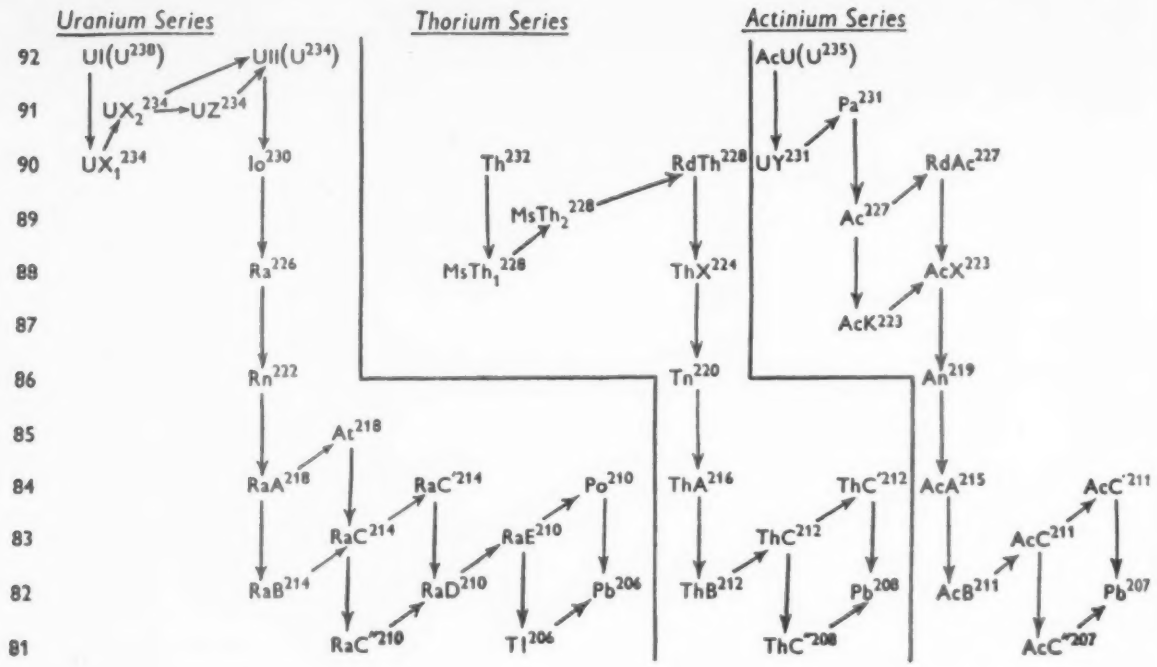

The sequence of the radioactive transformations.

(2) Thorium. The thorium series consists of thorium (mass 232) as the parent substance with lead (mass 208) as the stable end product.

(3) Actinium. The actinium series consists of actinouranium (mass 235) as the parent substance and lead (mass 207) as the stable end product.

Artificial. Shortly after the discovery of radioactivity it was noticed that material placed in close contact with a radioactive substance becomes radioactive. This phenomenon is called induced or artificial radioactivity. Induced radioactivity depends solely upon the nature of the original radioactive source and not upon the material receiving the activity. Artificial radioactivity is due to the absorption of a disintegrating product which is radioactive.

With the development of accelerators and nuclear reactors many different radioactive materials have become available. By artificial transmutation techniques a well developed neptunium series, including several trans-uranium species, has been prepared and investigated. The neptunium series consists of uranium (mass 233) as the parent substance and bismuth (mass 209) as the stable end product.

RADIATION CHARACTERISTICS

Types of Radiation

Radioactive isotopes in disintegrating, emit *alpha, beta* and *gamma* rays.

Alpha rays are high energy particles having a positive charge. They have a large mass and therefore cannot penetrate great thicknesses of matter. They are deflected by magnetic and electrostatic fields. Alpha rays cause intense ionization as they traverse a gas. The speed at which alpha rays travel varies with the radioactive source from which they are emitted, but generally is between 1/15 and 1/10 of the velocity of light. Alpha particles are emitted from sources with energies as high as 8 million electron volts. The actual range in air over which alpha particles can ionize is very short, never more than 8.6 centimeters. Alpha rays are readily absorbed by solids; they are completely cut off by a sheet or two of ordinary paper and they cannot get through 0.1 mm of epithelial tissue. An example of an isotope which emits alpha rays is samarium.[148]

Beta rays are high speed electrons ejecting from radioactive substances with velocities which cover a wide range—some exceeding 9/10 of the velocity of light. They are also deflected by magnetic and electrostatic fields. A beta particle may carry a negative charge (negatron) or a positive charge (positron). Beta rays ionize gases to a lesser extent than alpha rays. Beta rays are of small mass and travel at high speeds. They are much more penetrating than alpha rays. The fastest beta rays will pass through several millimeters of a low density metal or of tissue and traverse as much as ten feet of air before they are stopped. An example of an isotope which emits beta rays is phosphorus.[32]

Gamma rays have no mass and carry no electric charge. They are electromagnetic waves of the same nature as x-rays, but generally are of shorter wave lengths. The wave length depends on the radioactive source and for a given source more than one wave length is emitted. For example, radium C emits waves as long as 0.2 angstrom and some as short as 0.0056 angstrom. Gamma rays are so penetrating that some will not be absorbed by 10 cm. of lead. Muscle tissue, 2 centimeters thick, reduces the intensity only 5 percent and the rays emerge with over 60 percent their original intensity after penetrating 20 centimeters of tissue. Gamma rays ionize a gas through which they pass. This ionization is caused by an emission of secondary beta rays which results when gamma rays penetrate matter. Secondary beta rays may have velocities high enough to enable them to traverse a few millimeters of tissue or several meters in air before being stopped. When gamma rays penetrate matter, some scattering takes place, the amount depending on (1) the scattering material and (2) the quality of the primary beam. The intensity of a primary beam is reduced as it penetrates a layer of matter because of scattering and true absorption. An example of an isotope which emits gamma rays is iodine.[131]

Detection of Radiation

Charged particle radiations ionize gases through which they travel. These particles include alpha and beta rays, high velocity ions such as protons and deuterons.

Uncharged radiations—such as gamma rays and neutrons—produce charged secondary particles by their collision with absorbing materials; therefore, these charged secondary particles are capable of ionizing gases.

The detection of nuclear radiations is essentially the quantitative determination of the ionization produced by charged particles. Many instruments have been devised for detecting radiation. The following will serve to point out the various principles upon which most of the detection instruments are based:

1. Ionizing particles passing through an enclosed gas saturated with vapor are made visible by the condensation of water droplets on the ions produced. The cloud chamber operates on this principle.
2. Ionizing particles will activate the emulsion of a photographic plate even in the absence of light. This is the basis for autoradiography. The commonly used film badge illustrates this technique.
3. Ionizing rays cause ionization of the air in a chamber consisting of electric plates on two sides. The ions are driven to one of these plates which is attached to a measuring instrument (electrometer). The ionization chamber and electroscope are based on this principle.
4. Particle counting utilizes one of the following principles:
   a. Vacuum tube amplification of the original ionization produced by an alpha particle or proton. The linear amplifier utilizes this principle.
   b. Preliminary amplification in the ionization chamber through ionization by collision, followed by vacuum tube amplification. The proportional counter utilizes this principle.
   c. The original ionization triggers a discharge in the ionization chamber which is detected by a simple vacuum tube amplifier. The Geiger-Muller counter utilizes this principle.

Radioactive Disintegration

Radioactive elements disintegrate in a definite sequence until stable configurations of the atoms are attained. Radioactive elements spontaneously give off alpha, beta, and gamma rays—resulting in the loss of mass, charge, and energy. When an alpha particle is released from the nucleus, the element loses four mass units and two charge units. If a beta particle is ejected from the atom, the atomic weight remains unchanged but the atomic number is increased by one. When a gamma ray is given off, the element neither loses nor gains atomic weight or atomic number but a loss of energy occurs. (See Table 1).

Half-life is the length of time required for a given quantity of radioactive isotope to decrease to half of its original amount by radioactive disintegration. When 50 percent of the remaining radioactive atoms have disintegrated, a second half-life has expired, leaving only 25 percent of the original activity. For example: you receive a shipment of radioactive gold (half-life 2.7 days) which contained 100 millicuries at the time of assay (zero hour). In 2.7 days after zero hour there would remain only 50 millicuries of radiogold. Then, in another 2.7 days (or 5.4 days from zero hour) there would remain only 25 millicuries of radioactive gold, and so on. After six or seven half-lives have expired only a small amount of radioactivity remains.

Unit of Radioactivity

The Curie is the unit used to measure quantitatively the radioactivity of isotopes. The Curie is the quantity of radon in radioactive equilibrium with one gram of radium. Radon is a radioactive element obtained by the disintegration of radium. The disintegration rate is 3.7×10^{10} nuclei disintegrations per second per gram of radium.* The

* As defined by the International Radium Standard Commission in 1931.

Curie represents that quantity of radioactive material having the same number of disintegrations per second as one gram of pure radium.

The millicurie represents 1/1000 of a Curie or 3.7×10^7 disintegrating nuclei per second. The microcurie represents 1/1000 of a millicurie or 1/1,000,000 of a Curie. For example, the therapeutic dose of radioactive gold may be as high as 200 millicuries; whereas, a diagnostic dose of radioactive iodine may be as little as 5 microcuries.

RADIATION HAZARDS

Effects of Over-Exposure

The controlled use of radioisotopes may serve man well; but, improperly controlled radiation may be extremely hazardous. Excessive exposure to ionizing radiation will destroy living tissue. The mechanism by which radiation exerts its toxic action on living cells is still controversial.

Overexposure to radiation may cause (a) a decrease in the white blood cells, (b) destruction of the bone marrow, (c) loss of hair, (d) cataracts of the eye, (e) sterility and (f) nausea and vomiting.

Radioactive material may enter the body through inhalation, through the skin, or by way of the digestive tract. A chronic toxicity may result from the accumulation of radioactivity on contaminated hands, cigarettes, cosmetics and other items, brought in contact with the mouth.

The importance of possible genetic changes in future generations due to overexposure to radioactivity has not yet been established.

Protection from Radiation

Protective shielding against radioactive isotopes is designed to prevent excessive ingestion, inhalation, absorption, or external exposure to radiations.

Safeguards necessary to prevent over-exposure are (1) proper ventilation, (2) proper shielding with lead or other suitable material, (3) adjustment of maximum distance between radioactive source and the personnel, and (4) limiting the time of exposure.

Protection from substances emitting only alpha and soft beta rays is simple. Ordinary glass will shield alpha rays and low energy beta rays. High energy beta rays are more dangerous and require material other than glass as a shield. Lucite shields beta rays. Gamma rays are the most dangerous of the three. Lead is one of the better shielding materials for gamma radiation. Iron, aluminum, or concrete also afford protection from gamma rays.

The thickness of material required to safely shield personnel from radiation depends on (1) the activity of the radioisotope, (2) the working distance of the personnel from the radioactive source, (3) the hours of exposure per day, and (4) the type of absorber used as the shield.

RADIOACTIVE ISOTOPES

Review of Atomic Structure

To visualize an isotope chemically, it will be helpful to review the structure of the atom. The atom is composed of protons, electrons and neutrons.* The nucleus of the atom consists of the protons and the neutrons; whereas the electrons are arranged in a planetary orbit around the nucleus. Atoms of the same element have an equal number of protons and electrons. Different elements differ in their number of protons and electrons. The number of protons and neutrons within the nucleus determines the atomic weight of an element; whereas, the number of protons determines the atomic number. The following example will serve to illustrate these points:

Lithium^6

3 protons	= atomic number 3
3 protons + 3 neutrons	= atomic weight 6
3 planetary electrons	

The chemical properties of the atom vary with the number and arrangement of the electrons in the planetary orbits.

Isotopes

Atoms of the same element may have different numbers of neutrons in the nucleus—this changes the mass or atomic weight—but the number and arrangement of orbital electrons remain unchanged. These atoms have the same chemical properties as their parent atom but have different atomic weights. These atoms are called isotopes. Lithium 8 is an isotope of lithium.^{6}

Lithium^8

3 protons	= atomic number 3
3 protons + 5 neutrons	= atomic weight 8
3 planetary electrons	

Types of Isotopes

There are two types of isotopes—stable and radioactive. The stable isotope does not produce electromagnetic radiations and does not disintegrate. The radioactive isotope, on the other hand, exhibits the periodic emission of electrically charged particles resulting in the spontaneous disintegration of atomic nuclei until a stable state is reached.

* For simplicity, positrons, mesons, neutrons and photons are not mentioned.

PRODUCTION OF ISOTOPES

Since the introduction of nuclear reactors and the development of high voltage particle accelerators, the production of a large number of radioisotopes has been accomplished by bombarding stable elements with neutrons, protons, or other particles.

All artificially produced nuclear reactions are initiated by the capture of a particle or gamma ray by the nucleus and end with the ejection of one or more particles or gamma rays.

Nuclear reactions may be classified by the name of the projectile which initiates the reaction and the ejected particle. The projectiles may be gamma rays (γ), alpha particles (α), neutrons (n), protons (p), deuterons (d), tritons ($_1H^2$) (t); the ejected particle may be any one, or more than one, of these. The types of reactions are often designated by listing the projectile and the ejected particle. For example, an n, γ reaction indicates that the target element is bombarded by a neutron (projectile) and upon capturing this neutron emits gamma radiation (ejected particle).

Many radioisotopes are produced in the nuclear reactor but some isotopes can only be produced by accelerators such as the cyclotron. Radioisotopes are produced in the nuclear reactor by three main reactions:

(1) The (n, γ) reaction. The nucleus of the target element is bombarded by a neutron. Upon capturing this neutron the nucleus of the target element increases in weight by one mass unit. This element then emits gamma radiation and yields a radioisotope of the target element. For example:

$$_{11}Na^{23} + {}_0n^1 \longrightarrow {}_{11}Na^{24} + \gamma$$

(2) The (n,p) reaction. The nucleus of the target element is bombarded by a neutron and then emits a proton. The atomic number of the target element is reduced by one and the element is transmuted into the next lower element in the periodic table. For example:

$$_{16}S^{32} + {}_0n^1 \longrightarrow {}_{15}P^{32} + p$$

The (n, α) reaction is of the same type as the (n,p) reaction except that an alpha particle is emitted instead of a proton.

(3) Beta-decay of irradiated material. The nucleus of the target element captures a neutron. The newly formed isotope decays with the emission of a beta particle to form the required element. For example:

$$_{52}Te^{130} + {}_0n^1 \longrightarrow {}_{52}Te^{131} + \gamma$$
$$_{52}Te^{131} \longrightarrow {}_{53}I^{131} + \beta$$

The bombardment of a given nuclide (isotope) with one type of nuclear particle of one energy may lead to a variety of products. The Bohr theory suggests that a given compound nucleus may break up in several ways. For example, bombarding Al^{27} with fast neutrons (about 10 Mev.) produces a number of radioactive products; according to Bohr's theory the $_{13}Al^{28}$ may break up in any one of the following ways:

$$_{13}Al^{27} + {}_0n^1 \longrightarrow {}_{13}Al^{28} \longrightarrow \begin{cases} {}_{13}Al^{26} + 2\,{}_0n^1 \\ {}_{13}Al^{28} + \gamma \\ {}_{12}Mg^{27} + {}_1H^1 \\ {}_{11}Na^{24} + {}_2He^4 \end{cases}$$

A radioactive isotope available in pure form is designated "carrier-free." In the aluminum reaction illustrated above, there is a mixture of three aluminum isotopes: $_{13}Al^{27}$, $_{13}Al^{28}$ and $_{13}Al^{26}$. Since these aluminum isotopes have the same number of planetary electrons, their chemical properties are identical. Therefore, these substances cannot be separated by chemical means. Therefore, $_{13}Al^{28}$ is not carrier-free.

The specific activity is the radioactivity per unit weight of radioactive material. The specific labeled content is the ratio of the number of radioactive atoms to the total number of isotope atoms. In the above cited aluminum reaction the specific labeled content would be:

$$\frac{Al^{28}}{Al^{27} \qquad Al^{26}}$$

High specific activity is important in tracer experiments because the radioisotopes may be diluted to a greater extent and still can be measured reliably.

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POLYVINYLPYRROLIDONE IODINE

a three year observation of a new topical germicide

by ROBERT C. BOGASH

FROM THE FIRST SPECIFIC REFERENCES to the use of iodine[1,2] on wounds, iodine has been proved a useful germicide. It has been shown to act against a variety of microorganisms including bacteria, viruses, protozoa, fungi, yeasts, and spores. Yet iodine has not been widely employed because of the problems inherent to the use of free iodine, such as toxicity to the tissues, instability, and insolubility in water. Polyvinylpyrrolidone iodine (PVP-I) is a detoxified form of iodine, nonirritating, film-forming and non-staining. It is both soluble and stable in water, and yet retains the chemical and germicidal properties of iodine.[3]

Iodine has long been recognized as a non-selective germicide. It was initially included in the *U.S.P.* in 1860 and in the *British Pharmacopoeia* in 1885. "One of the most striking characteristics of iodine as a germicide is its uniformity of action on different species of microorganisms."[4] Walter, in the same report, points out that "aqueous solutions are more effective germicides, do not irritate the tissues, and are painless." *In vitro* experiments,[5] reporting on the relationship between killing and stasis of miroorganisms in tissues, indicate that iodine kills immediately rather than by prolonged stasis. This work was done employing concentrations of iodine and other germicides that are frequently used in practice. This was later confirmed by Salle and Catlin[6] who observed that effective concentrations of iodine represented true killing values, and that no bacteriostasis was involved. They also reported that the highest dilution of iodine, 1:20,000, killing within one minute was the same as for ten minutes, a property not shared by any of the other antiseptics. Other workers, Salle, *et al* [7,11] McCulloch and Fuller,[8] Gershenfeld and Witlin,[9] Chambers *et al*,[10] also have reported on the bactericidal activity of iodine.

Iodine has been found to possess both a high fungicidal and fungistatic efficiency against a variety of fungi.[12] It has been cited to possess fungicidal activity for *Trichophyton gypseum, Monilia albicans*,[14] and *Epidermophyton inguinale*,[15] as well as various other species of monilia, torula, epidermophyton, trichophyton, and saccharomyces.[13,16]

While the virucidal properties have not been studied or documented as comprehensively, they are known. In fact, these properties have recently been the subject of renewed interest and extensive study.[25] Viruses which have been found to be affected by iodine are those of vaccinia, rabies, herpes simplex, trachoma and myxoma[18] as well as influenza and Newcastle disease.[26] Gershenfeld[17] proved low concentrations of iodine to be very effective against the viruses of poliomyelitis.

Polyvinylpyrrolidone

Polyvinylpyrrolidone (PVP) is a water-soluble polymer which is physiologically acceptable to both animals and humans. It has been employed

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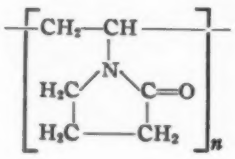
in the United States and Europe as a plasma volume expander, drug vehicle (for its repository effect), and as a suspending agent because of its protective colloid effect. PVP is also reported to penetrate the hair follicle. This phenomenon has been termed a "substantive effect".



Polyvinylpyrrolidone (PVP)

PVP, made by the polymerization of N-vinyl pyrrolidone, has the ability to combine with many materials, frequently changing their properties. Quite often this combination markedly changes the physical and toxicological properties of the original material.[3]

Iodine is strongly "complexed" by PVP. This "complex" is considered to be an iodophor. In Reddish, Gershenfeld[18] describes the characteristics of iodophors as a "display of enhanced bactericidal activity of iodine, a reduction of vapor pressure, odor and staining to almost the vanishing point, and they can be readily diluted with water." The "complexing" of PVP and iodine eliminates, or at least minimizes, most of the difficulties previously experienced with the use of free iodine. The oral toxicity of iodine is reduced by the PVP and further, this "complexing" also markedly reduces irritation to the tissues.

Upon drying, PVP-Iodine solutions form films which may remain as a protective covering or, if desired, can be removed with water. PVP-Iodine may be washed from linens and other natural fabrics with water without leaving a stain.

Microbiology, Skin Sensitivity, Toxicology

Studies were conducted to determine whether or not iodine in the form of PVP-Iodine loses any of its killing power for microorganisms. Brief mention shall be made to some of the studies done.

1. PVP-Iodine was tested as an agent for water disinfection using Tincture of Iodine, U.S.P., as a reference material. The studies indicate that iodine in the form of PVP-Iodine is as effective as the iodine in the official tincture.[19]

2. Employing a "capacity method"[22], PVP-Iodine sterilized 35 increments (70 ml. broth) while the control solution sterilized only 16 increments (32 ml. broth). From this study it appears that solutions of PVP-Iodine are more effective than aqueous solutions of elemental iodine of the same titratable iodine concentration.[19]

3. Bactericidal efficiency tests were performed in accordance with the Food and Drug Administration technique[20] employing *Micrococcus pyogenes* var. *aureus*. This test method indicates that dilute PVP-Iodine solutions are superior to dilute aqueous and alcoholic solutions of the same titratable iodine concentrations.[19]

4. Employing A.O.A.C. phenol coefficient procedures, three prepared formulations*, each containing PVP-Iodine as the active ingredient, were tested against frequently used products available on the open market.[24] The three forms of PVP-Iodine tested were: a buffered aqueous solution (1 percent available iodine), an hydroalcoholic buffered solution (0.75 percent available iodine), and an hydrophilic ointment (1 percent available iodine). The comparative products included nitrofuran ointment (Furacin), a zinc undecylenate-undecylenic acid ointment (Desenex), thimerosal solution 1:100 (Merthiolate), a cetylpyridinium chloride mouth wash (Cepacol), a quaternary - ammonium - chlorothymol solution (Bactine), merbromin aqueous solution (Mercurochrome), and several popular mouth washes including Listerine and Lavoris. The organisms used were *Streptococcus pyogenes, Pseudomonas aeruginosa, Escherichia coli, Micrococcus pyogenes* var. *aureus, Candida albicans,* and *Trichophyton mentagrophytes.* In all of the testing procedures, the formulations containing PVP-Iodine as the active ingredient killed microorganisms faster and were superior to the other materials tested.

Sensitivity

5. Using the Schwartz method[23] of skin testing, employing 200 human subjects, it was found that none of the males or females reacted to PVP-Iodine (10 percent available iodine) in either the first or second application. From these results

*Preparations containing PVP-Iodine as the active ingredient supplied by the Isodine Pharmacal Corporation, Dover, Delaware.

it appears that the samples studied were neither primary irritants nor did they tend to sensitize.[19]

6. Eye irritation studies[19] were conducted on 10 guinea pigs. One-half (0.5) ml. of an aqueous solution of PVP-Iodine (1 percent available iodine) was instilled into the left eye of each animal. The eye was observed daily for two weeks using the right eye as a comparison. A slight reddening of the conjunctival sac appeared following each instillation and disappeared from 4 to 6 hours later. The same procedure was repeated two weeks later, on the same animals, with the same results.

Acute Oral Toxicity[21]

Aqueous solutions of PVP-Iodine were introduced into the stomachs of white albino rats by means of a tube. Diluted Lugol's Solution of equivalent iodine concentration was used as a control.

PVP-Iodine

(*2.51% available iodine*)

LD_{50}—24 hours	990	mg./Kg.
LD_{50}—48 hours	890	mg./Kg.
LD_{50}—72 hours	880	mg./Kg.

Diluted Lugol's Solution

(*2.49% available iodine*)

LD_{50}—24 hours	200	mg./Kg.
LD_{50}—48 hours	172	mg./Kg.
LD_{50}—72 hours	152	mg./Kg.

At post-mortem, with PVP-Iodine no hemorrhages were observed and no other gross pathology was noted. With diluted Lugol's Solution, nearly all animals exhibited a hemorrhagic gastritis. No other gross pathology was noted.

Observations

While the author has been acquainted and associated with the use of PVP-Iodine for at least 5 years*, this preliminary report covers the last 3 years, wherein, because of its expanded application, the clinical results have been best observed.

PVP-Iodine solutions and later prepared formulations containing PVP-Iodine as the active ingredient have been used in the Outpatient Department, Inpatient services, and private practice. To date, a total of 5,900 patients, ranging in age from premature infants to 90 years, have been treated with this material. It has been found effective in treating a variety of infections frequently encountered in the practice of otolaryngology, orthopedics and orthopedic surgery, obstetrics and gynecology, oral surgery, pediatrics, surgery, and dermatology.

Among the conditions that have been treated in otolaryngology and pediatrics were cases diagnosed as oral moniliasis (thrush), pharyngitis, tonsillitis, stomatitis, and gingivitis. The clinical response to PVP-Iodine preparations has been reported as good to excellent. In orthopedics, it has been used for well over 18 months for the preoperative preparation of the site of expected incision, for disinfection of the skin prior to intra-articular needling procedures, i.e., aspiration or instillation of sterile hydrocortisone acetate suspension. It has also been used for the disinfection of wounds, including compound fractures as well as in the treatment of decubitus ulcers. There has not been one case of postoperative infection on this service in the last year, nor has there been any clinical sign of infection following several thousand needling procedures.

In dermatology, the ointment has been used as an agent for mycotic infections, ammoniacal dermatitis with secondary infection, and diagnosed papillary urticaria.

In obstetrics and gynecology, PVP-Iodine solutions (0.1 percent to 0.5 percent available iodine) have been used as a douche, in the treatment of conditions diagnosed as vaginal moniliasis, trichomonas vaginalis vaginitis, and leucorrhea. Its use in these conditions is reported good to excellent with particular note of the quick symptomatic relief of pruritus that attends its use. In oral surgery, it has been used (in concentrations of 1 percent available iodine) for the routine preparation of soft tissue prior to surgery and the injection of a local anesthetic, as well as for suppurative, traumatic, allergic or mycotic lesions. In dilute solutions (0.02 percent available iodine) it has been used as a pressure spray and also for the irrigation of operative sites, during surgery. It has also been used in the treatment of aphthatous ulcers with reported success.

Side Effects

Two cases of idiosyncrasy to PVP-Iodine have been reported. Both reactions were manifested as a dermatitis. Both responded to therapy within 7 days. No signs of systemic toxicity or iodism have been noted. Of the total number of patients treated, there has been no clinical evidence of retardation of healing or iodine "burn".

*Philadelphia General Hospital, Mt. Sinai Hospital, Philadelphia and the Memorial Hospital, Wilmington, Delaware.

Summary

Observations over a 3-year period indicate that PVP-Iodine is a safe and useful agent in the treatment of various infections. Employed as a topical antiseptic, in several formulations, it has been used on 5,900 patients, in the Outpatient Department, Inpatient services, and private practice.

PVP-Iodine, a detoxified, nonirritating, and film-forming compound is reported to afford distinct symptomatic relief of pain, itching, and dryness when used as a mouth wash. Bacterial infections responded rapidly to PVP-Iodine therapy as did diagnosed mycotic infections. The solution and ointment have been used in the emergency treatment of lacerations and abrasions, as well as over sutures on the face, hands and arms, without any clinical sign of retardation of healing, or iodine "burn" reported even when bandaged.

Of the 5,900 patients treated, two idiosyncrasies have been reported. Both were manifested as a dermatitis, which subsequently responded to supportive therapy in 7 days. No signs of systemic toxicity, or iodism have been reported.

Conclusion

It is felt that the "non-selective" nature of PVP-Iodine to kill microorganisms, its minimal toxicity, and the clinical results reported under various conditions of use make PVP-Iodine preparations valuable adjuncts in both the hospital and in private practice.

Acknowledgments

For his unfailing aid and advice, special acknowledgment is made to the late Dr. Herman Shelanski, inventor of PVP-Iodine, who initially supplied this material.

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ASHP President Parker and fellow officers at the Detroit Meeting.
Left to right: Gloria Niemeyer Francke, Sister Mary Berenice, Paul Parker, and Milton Skolaut.

APHA-ASHP ANNUAL

MEMBERS OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, including delegates from 34 of the Society's 45 affiliated chapters, met in Detroit, Michigan, April 8, 9, and 10, for the 1956 Annual Meeting. Held in conjunction with the Convention of the American Pharmaceutical Association, hospital pharmacists attended meetings of the parent organization and affiliated groups throughout the week. This is believed to be one of the largest meetings held by the SOCIETY with approximately 200 in attendance throughout. Participation in all activities from the Opening Session of the House of Delegates on Sunday throughout the Final Session which ended at nearly 7 P.M. on Tuesday, indicated growing interest in hospital pharmacy and the affairs of the SOCIETY. The Business Sessions and the Program, as well as the special activities arranged by the Michigan Society, all proved successful. This year's Annual Meeting was presided over by President Claude Busick and the Program was in charge of Mr. Leo Godley.

Also playing an active part in the total planning for the Annual Meeting were the members of the Michigan Society under the leadership of Mr. Don Melcher, Chairman of the local Convention Committee. Numerous other hospital pharmacists in the local area actively participated in making arrangements for special events.

The H.A.K. Whitney Award Dinner, held for the first time during an Annual Meeting of the national society, was a highlight of the week's events. The Award, presented to Dr. George F. Archambault for outstanding contributions to hospital pharmacy, was made at a dinner attended by more than 250 people on Monday evening. Also attending the dinner in an official capacity were Dr. Sarah Hardwicke representing the Council on Professional Practice of the American Hospital Association, Mr. M. R. Kneifl of the Catholic Hospital Association, Miss Love Chabak of the Canadian Society of Hospital Pharmacists, and President Claude Busick, who spoke on behalf of the ASHP. Also present was Mr. Harvey A. K. Whitney, first chairman of the ASHP and in whose honor the Award was established. Mr. Whitney spoke briefly on some of the background concerned with the development of the SOCIETY and expressed appreciation for the honor given him as well as the continuing enthusiasm of the hospital pharmacists throughout the country. The Award was presented by the president of the Michigan Society of Hospital Pharmacists, Mr. Harold Tayler and Dr. George F. Archambault responded

with a dissertation of "Ethical Standards and Professional Conduct of the Hospital Pharmacist." In his Address, he called on leaders of hospital pharmacy to consider developing an enforceable code of ethics "to express the social conscience of the group, to guide the 'young' in the profession and afford inspiration to the 'oldsters' in the profession."

Awards Presented

In addition to the H.A.K. Whitney Award, note should be made of other honors received by hospital pharmacists during the convention week.

At the SOCIETY's First Session, Dr. Alex Berman, Acting Secretary of the American Institute of the History of Pharmacy, presented two-year gift memberships to the Institute, along with an autographed copy of *Pharmacy's Part in Society,* to two hospital pharmacists for outstanding contributions on the history of their respective affiliated chapter. The awards were presented to Miss Doris Hawkins (in absentia) of the Arizona Society and to Mr. William Whitcomb of the Rochester Area Society of Hospital Pharmacists. On presenting the awards, Dr. Berman read a letter of commendation from Dr. George Urdang, Director of the Institute.

Another award was presented by Mr. J. Warren Lansdowne, Chairman of the Public Relations Committee of the American Pharmaceutical Association. The award, presented for the best hospital pharmacy display during National Hospital Week was received by Sister Mary Jeanette, Chief Pharmacist at Mary Immaculate Hospital in Jamaica, New York. On making the presentation, Mr. Lansdowne called attention to the fact that Sister Mary Jeanette has been in hospital pharmacy practice for forty-seven years, is a recipient of the Lascoff Award, and is a Past Treasurer and member of the Executive Committee of the SOCIETY.

Another hospital pharmacist honored was Sister Mary Oswalda of St. Joseph's Children and Maternity Hospital, Scranton, Pennsylvania. She received the first prize for the best pharmacy display in a hospital during National Pharmacy Week. This award was presented at the First General Session of the American Pharmaceutical Association. The second prize, a certificate of merit, was

...MEETING . . . DETROIT

A view of one of the General Sessions held at the ASHP Annual Meeting in Detroit.

awarded to Miss Cynthia Wu, St. Luke's Hospital, Cleveland, Ohio and the third prize, also a certificate of merit, was awarded to Mr. Frank F. Stencil, Montefiore Hospital, Pittsburgh.

House of Delegates and Business Sessions

The 1956 Annual Meeting of the SOCIETY brought 37 delegates representing 34 of the SOCIETY's affiliated chapters; eight of the ten members of the Executive Committee; and eight of the eleven chairmen of special committees; making a total of 53 voting members in the House at the meeting on Sunday afternoon. In addition, approximately 75 other members attended and participated. This was probably one of the most active meetings of the House of Delegates ever held and it revealed the need for a study of the organizational structure of the ASHP with particular reference to its relationship to the affiliated chapters. At the panel which was moderated by Mr. Grover C. Bowles, a past president of the SOCIETY, a number of delegates brought out some of the problems relating to membership, programming, and relationships with the national organization. Delegates were urged to take an active part in the deliberations at the Annual Meeting and a representative from each affiliated chapter was given a complete set of reports presented by officers and committee chairmen at the General Session on Monday.

ABOVE: *ASHP President Claude Busick who presided at the Detroit Meeting.* BELOW: *President Harold Tayler of the Michigan Society of Hospital Pharmacists presents the Whitney Award to Dr. George F. Archambault for outstanding services to his profession.*

Another highlight of the meeting of the House of Delegates was the Address of the President-Elect, Mr. Paul Parker. In developing his plans for the ensuing SOCIETY year, Mr. Parker divided his remarks into two categories—first, recommendations concerning the improvement of hospital pharmacy as a profession and second, suggestions concerning the SOCIETY as an organization and working toward these improvements. He pointed out "that a professional organization should have as its motivation the primary concern of the profession itself rather than the interest of individuals or groups of individuals who practice the profession."

At the First Business Session on Monday morning, members ofthe SOCIETY heard reports from each of the officers, the chairmen of the four standing committees and from ten chairmen of the special committees. In addition, Dr. Robert P. Fischelis, Secretary of the A.Ph.A. and Chairman of the Policy Committee of the Division of Hospital Pharmacy, and Dr. Don E. Francke, Director of the Division of Hospital Pharmacy, reported to the SOCIETY.

Actions taken by the ASHP at this Annual Meeting will serve as a guide for future activities. The full text of resolutions will appear in the July-August issue of THE BULLETIN. However, the following summary will give members information regarding actions taken by the SOCIETY at the 1956 Annual Meeting.

—Resolved to encourage schools of pharmacy to make available in their undergraduate curriculum courses leading to a major in hospital pharmacy.

—Asked that special attention be given in the institute programs to providing for sessions for uniform service personnel.

—Extended appreciation to the United States Public Health Service for the assistance given to the speciality of hospital pharmacy as evidenced by the recent grant made to the American Pharmaceutical Association for a study of pharmaceutical services in hospitals.

—Expressed appreciation to the Lederle Laboratories for making funds available for research in hospital pharmacy.

—Resolved that the Committee on Narcotics, Hypnotics, Ethyl Alcohol, etc. be expanded and given a new name such as "Committee on Hospital Pharmacy Laws, Regulations, and Legislation."

—Asked that the SOCIETY explore the possibility of participation in the Annual Meetings of the national Hospital Association.

Panel on hospital pharmacy internships showing present interns and recent graduates with Mr. Herbert Flack and Mrs. Evlyn Scott, moderators of the panel, standing.

—Again urged all members of affiliated chapters to join the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and asked that the Executive Committee take proper action with regard to those chapters in which all members are not affiliated with the national organizations.

—Requested that the new interpretations of the narcotic laws as being prepared by the Committee on Narcotic Regulations be published in THE BULLETIN as soon as possible and disseminated in final form to the various groups concerned.

—Approved the new revised forms as presented by the Committee on Narcotic Regulations.

—Asked that the Secretary report at the Annual Meeting regarding actions taken on resolutions each year.

—Asked that local affiliated chapters of the ASHP be encouraged to participate in the A.Ph.A. Building Fund Drive.

—In addition to those actions listed above, the SOCIETY also expressed appreciation to a number of organizations and individuals who have made outstanding contributions to our activities during the past year. Further, a number of resolutions were referred to the Executive Committee for study.

Also of significance is the fact that at a meeting of the SOCIETY'S Executive Committee immediately prior to the Convention, the group voted to pledge $1,000 toward the A.Ph.A. Building Fund. As noted above, a recommendation was also made to urge the ASHP affiliated chapters and individual members to contribute.

The Executive Committee also accepted responsibility for the selection of recipients of funds under a grant made by the Lederle Laboratories Division of American Cyanamid. Funds are designated for research in the various aspects of pharmacy services in hospitals, and will be available to hospitals, and students in hospital pharmacy and related fields.

Program

The total program, including all papers presented at this year's Annual Meeting, was successful in every respect. A wide variety of subjects were presented by leaders in hospital pharmacy, the hospital field, and allied groups. Of particular note is the fact that representatives from both of the national hospital organizations, the American Hospital Association and the Catholic Hospital Association, participated. Each expressed interest in the activities of the ASHP and pledged cooperation in carrying out our work. A complete listing of the papers presented at the Annual Meeting was included in the January-February, (1956) issue of THE BULLETIN and, when feasible, papers will be published in a forthcoming issue.

New Officers and Nominees

New officers of the ASHP installed at the FINAL SESSION on Tuesday included *President,* Paul Parker, Washington, D. C.; *Vice President,* Milton Skolaut, Bethesda, Md.; and *Treasurer,* Sister Mary Berenice, St. Louis, Mo. Sister Mary Berenice has been elected for a three-year term beginning with this Annual Meeting. Other members who will serve on the Executive Committee are listed on page 162 of this issue of THE BULLETIN.

Nominations for officers of the American Society of Hospital Pharmacists for the 1957-1958 term are as follows: *For President*: Leo F. Godley, Bronson Methodist Hospital, Kalamazoo, Mich. and Charles G. Towne, Veterans Administration Center, Los Angeles, Calif. *For Vice President*: Charles Barnett, St. Luke's Hospital, Jacksonville, Fla. and Ludwig Pesa, St. Mary's Hospital, Passaic, N. J.

therapeutic TRENDS

edited by WILLIAM JOHNSON

WIN 5047 — In Treatment Of Strongyloidosis

WIN 5047, N-(2,4-dichlorobenzyl-N(2-hydroxyethyl) dichloroacetamine, is under clinical evaluation as a nonmetallic amebacidal compound. In the course of investigation, patients were encountered concomitantly parasitized with *E. histolytica* and *Strongyloides stercoralis* in whom this agent apparently eradicated both the protozoa and the nematode.

McHardy *et al.* reports in *J. Louisiana Med. Soc.* No. 1:27 (Jan.) 1956 the establishment of an initial therapeutic regimen of 750 mg. WIN 5047 three times a day for 10 days. Resistance and recurrence were encountered. Since the compound was well tolerated and showed no toxicity in extended study the dosage schedule was increased to 4,000 mg. daily for 20 days. The compound has proved to be more efficient and innocuous than gentian violet in a limited study. WIN 5047 was supplied for this study by Winthrop-Stearns, Inc. as Mantomide.

Benactyzine — A Relaxant

Benactyzine hydrochloride, the hydrochloride of 2-dimethylaminoethyl benzilate, is a member of a group of anticholinergic substances and experimental work in Denmark suggests that it produces a state of emotional and physical relaxation without drowsiness. In the *Brit. Med J.* I:485 (Mar. 3) 1956, Coady and Jewesbury describe the results of a clinical trial of this drug.

In a group of 80 neurological patients, no effect of muscle tone and no significant relief of symptoms were produced by a two-weeks course of 2 mg. of benactyzine three times daily by mouth. Subjective improvement was reported after benactyzine by many patients. Similar improvement after inert control tablets was reported by almost the same number. No systemic toxic effects were observed, but transient psychological side effects occurred in 40 percent of 72 patients who received a dosage of 2 mg. All 8 patients who received 4 mg. showed such side effects. With single oral doses of more than about 6 mg. normal control subjects showed increasing thought blockade, impairment of concentration, slowness and clumsiness in carrying out complicated procedures, and general flatness of effects. Such symptoms developed within about 20 minutes and lasted up to about 1½ hours. A striking suppression on the normal rhythm of the EEG after administration of benactyzine has been demonstrated.

Salicylates — In Recurrent Urolithiasis

Urinary calculi recur in a significant number of patients, and presently accepted medical regimens for control of calcium-containing stones are not highly successful. It was confirmed experimentally that glucuronide enhances the solubility of calcium phosphate. Glucuronide normally occurs in small amounts in the urine, conjugated with various products of metabolism. Its excretion can be increased by the administration of compounds that are excreted as glucuronide conjugates. With a dosage of 2 gram of acetylsalicylic acid or of salicylamide daily, urinary glucuronide excretion was increased from two to four times. A series of 19 patients were studied by Prien and Walker and their findings are reported in *J. Am. Med. Assoc. 160*:355 (Feb. 4) 1956. They warn against the use of larger doses of salicylates because an undesirable increase in calcium secretion may be produced. The use for this purpose of acetylsalicylic acid-steroid hormone combinations is vigorously condemned. The use of salicylates to prevent recurrence of calcium-containing urinary calculi is a promising but as yet unproved therapy.

SKF 2599 — An Anticonvulsant

A clinical trial of a new anticonvulsant, 5,5-diphenyl - tetrahydroglyoxaline - 4 - one (SKF No. 2599), has been continued for a period of six months in 22 patients with grand mal or psychomotor seizures which were previously uncontrolled despite prolonged treatment with Dilantin and/or phenobarbital. The majority of patients were mentally retarded and 45 percent had cerebral palsy. The epilepsy was controlled completely in 12 (55 percent)of the 22 patients, and a practical level of control was obtained in 6 (27 percent). Among the patients whose seizures were well controlled, three had psychomotor epilepsy. The average optimal daily dose was 0.8 Gm. (20

mg./Kg.). Side effects, which resembled those produced by Dilantin, involved the central nervous system and the gastrointestinal tract; the incidence of gum hyperplasia, however, was minimal. Compared with existing anticonvulsant compounds, SKF 2599 has exhibited definite advantages in this preliminary clinical evaluation, and more extensive trial is recommended, particularly in non-institutionalized epileptic patients. This clinical trial was conducted by Milichap et al. and their results published in *Neurology* 5:700 (October) 1955.

Banthine — Preanesthetic Drying Agent

Banthine was used by Alver and Vander Wood as a preanesthetic drying agent in 150 children between the ages of four days and ten years. A formula to determine the dosage, based on weight of the child, was devised. Using this formula, drying of the respiratory tract was satisfactory in 93.3 percent of cases, and the drug was well tolerated by a vast majority of the children. However, the dosage proved inadequate for negro children. The advantages of the drug as a drying agent in children, as well as the side-effects, especially cardiovascular, are discussed. Five cases of overdosage and 3 cases of sensitivity to Banthine are presented. This work was publishel in *Anesthesiology* 17:73 (January) 1956.

Silicone Barrier Cream — A Decubitus Preventive

Bateman describes in the *Brit. Med. J. I*: 554 (Mar. 10) 1956 a method of preventing decubitus using a silicone barrier cream instead of the usual methods. The silicone barrier cream consists of 20 percent polydimethyl-siloxane in a water-soluble base. It has been found to be the most pleasant and economical in use. Observations over a period of six months show that it is at least as effective as usual methods. The saving in nursing time and labor justifies its continued use. Further trials using this method are in progress.

Mycolutein—An Antifungal Antibiotic

From the mycelium of a streptomycete exhibiting unusually broad inhibitory potency, a yellow crystalline compound was isolated. This previously undescribed compound has been named mycolutein. Mycolutein inhibits a variety of fungi at concentrations of the order of 1 mcg./ml. but shows no activity against a variety of bacteria. The constant melting point of the compound and countercurrent distribution experiments furnish some evidence of its essential purity. Chemical tests indicate an aromatic nucleus and unsaturation. This study was reported in *Antibiotics and Chemotherapy* 5:652 (November) 1955 by Schmitz and Woodside.

Sulfonamides and Hypoglycemia

During a clinical trial of the chemotherapeutic action of *p*-amino-benzene-sulfonamido-isopropyl-thiodiazole, Janbon and his associates noted that this substance produces a fall in the blood-sugar level which may be so profound as to lead to hypoglycemic coma. This clinical observation was confirmed by experimental studies in rabbits and dogs. Oral or subcutaneous administration to dogs results in hypoglycemia, the blood sugar falling to as low as 40 mg. per 100 ml. within five hours. A study of several thiodiazole derivatives was then undertaken. Non-sulfonamide thiodiazoles have no hypoglycemic action, but several compounds of the *p*-amino-benzene-sulfonamido-thiodiazole group lower the blood sugar in animals. Recently another sulfonamide compound, sulfanilyl-*n*-butlyurea, has been found to have a similar effect on the blood sugar level. With this background information, it was a natural step to ascertain the effect of this substance in diabetic patients. So far the evidence is insufficient for any definite conclusion about the pharmacological action of these compounds. They clearly open up a new approach to the study of carbohydrate metabolism and diabetes mellitus. The preliminary reports suggest that they may be useful in the oral treatment of elderly diabetics but not of young or acidotic patients. Further carefully planned clinical trials may determine the place of these sulfonamide compounds in the management of diabetes, and we hope that the trials will be completed before these powerful substances become widely available. This information appeared in *The Lancet I*:193 (January 28) 1956.

EDITOR'S NOTE. The Upjohn Company recently announced the following: A bacteriostatically inert aryl sulfonylurea originally synthesized in Germany, and which is now being intensively studied in this countrv. has been found to produce hypoglycemia in intact animals but not in depancreatized or alloxan-diabetic animals. Preliminary observations show that this compound is also orally effective in reducing hyperglycemia and glycosuria in patients with the adult form of diabetes mellitus. Less consistent beneficial effects can probably be expected in the juvenile type of diabetes, judging from observations known to date. The mechanism of this hypoglycemic action remains to be clarified. The Upjohn name for this compound is Orinase and they are developing this compound for this country. Orinase will not be commercially available for some time. While early clinical studies are encouraging, the decision as to whether or not to market it must of course await substantiation and verification by careful detailed investigation. Such work is now in progress, but will require many months to complete.

timely drugs

A.P.C. with Demerol Tablets

. . . have been released by Winthrop Laboratories. The combination provides a rapid, potent and prolonged level of analgesia with mild sedation, spasmolytic and antipyretic action for the relief of pain. Specific conditions in which A.P.C. with Demerol may be administered are: arthritis, neuritis, migraine, cardiovascular pain, gallbladder disease, renal colic, toothache, neoplasm, trauma, minor surgery, and instrumentation. Each tablet contains 200 mg. aspirin, 150 mg. phenacetin, 30 mg. caffeine, and 30 mg. Demerol hydrochloride. The usual adult dose is one or two tablets by mouth, repeated, if necessary, at intervals of from three to four hours.

Bonadoxin Drops

. . . is a combination of the antihistamine meclizine dihydrochloride and pyridoxine hydrochloride (vitamin B_6) in a pleasant tasting, lime-flavored suspension. Bonadoxin drops, a product of the J. B. Roerig and Company, Division of Chas. Pfizer and Company, is indicated in the treatment of infant colic, paroxysmal fussings and irritable crying in the hard-to-manage infant. It provides antihistamine action to relieve colic of possible allergic origin, anticholinergic activity to break the cycle of emotional tension and to relieve pain, resulting in a tranquilizing effect to calm the infant and permit sleep. It also protects against colic and infantile convulsive disorders resulting from pyridoxine deficiency.

Bonadoxin drops offer the advantages of providing a simultaneous attack against the three major symptoms of infant colic—nervous tension, intestinal spasm and pain; and freedom from atropine-like side effects, or barbiturate hangover and addiction. The drops are administered orally and may be mixed with formula or fruit juices if desired.

The preparation is supplied in 30 ml, plastic dropper bottles, each ml. containing 8.33 mg. meclizine and 16.67 mg. pyridoxine. (3 ml. Bonadoxin drops is equivalent to 1 Bonadoxin tablet in meclizine and pyridoxine content.)

Cathomycin

. . . a unique new antibiotic which has been shown to be highly effective against organisms resistant to all known antimicrobial agents, is now available from Sharp & Dohme, Division of Merck & Co.

Cathomycin (novobiocin, Merck) is derived from *Streptomyces spheroides,* and has proved to be highly effective, even in low concentrations, against *Streptococcus, Diplococcus, Corynebacterium, Pasteurella,* and against some resistant strains of *Proteus vulgaris.* No cross resistance has been reported with other currently used antibiotics. Further, synergistic bactericidal action has been demonstrated *in vitro* with penicillin, chlortetracycline, oxytetracycline, chloramphenicol, streptomycin, bacitracin, neomycin, streptothricin, and grisein.

Cathomycin is well absorbed following oral administration and tolerance to it has been generally very good. Indications for the drug comprise infections resistant to other antimicrobial agents and have inincluded cellulitis, recurrent and persistent carbuncles, various skin abscesses, postoperative wound infections, varicose ulcer, felons and paronychiae, and staphylococcic septicemia and enteritis. It is of particular value in connection with surgery since staphylococcus infections seem prone to complicate postoperative courses.

Sensitivity disks can be used to determine the relative effectiveness of Cathomycin against a specific infecting organism as compared with other available antibiotics. Disks are supplied in 2, 10, and 50 mcg. concentrations.

Cathomycin for oral administration is available as 250 mg. capsules in bottles of 16.

Co-Deltra and Co-Hydeltra

. . . Sharp & Dohme's brand of buffered prednisone and buffered prednisolone, is now available in multiple compressed tablets in a new strength of 2.5 mg. This new dosage strength provides twice as much antacid per mg. of steroid as does the 5 mg. strength and is recommended in cases where a higher antacid to steroid ratio may be desirable, such as for prolonged therapy.

Cordex Forte Tablets

. . . a new and more potent formula combining steroid and salicylate medication, is being marketed by the Upjohn Company.

The new form differs from Upjohn's original product, Cordex tablets, in that it contains three times as much prednisolone. Cordex Forte tablets have been found particularly useful for maintenance therapy in rheumatoid arthritis and various other painful conditions affecting the musculoskeletal system. Each scored Cordex Forte tablet contains 1.5 mg. prednisolone and 300 mg. acetylsalicylic acid, and is available in bottles of 100 and 500.

Cytellin Suspension

. . . an oral suspension of sitosterols for the control of hypercholesterolemia, has been released in limited areas by Eli Lilly and Company. Sitosterol, which differs only slightly in structure from cholesterol, combines with cholesterol in the intestine to form a physical complex that is highly insoluble and, as a consequence, the absorption of cholestrol is largely prevented. A sterol obtained from a variety of plant sources, sitosterol presumably interferes not only with the absorption of cholesterol contained

in food but also with the reabsorption of cholesterol secreted in the bile and through the walls of the intestinal tract. However, since the liver produces whatever amount is needed by the body, Cytellin does not lower the serum cholesterol concentration in individuals having "normal" levels.

Hypercholesterolemia is suspected by many heart specialists of being the "main culprit" in cardiovascular disease. Atherosclerosis, one of most serious of the cardiovascular diseases, is accompanied in most patients with elevated concentrations of cholesterol in the blood serum. Thus it is reasoned that prolonged control of hypercholesterolemia through Cytellin may prevent atherogensis. It is indicated in all conditions in which sustained reduction of hypercholesterolemia is desirable. There are no known contraindications to its use.

Cytellin is a palatable, lightly flavored suspension of 20 percent beta and dihydro-beta-sitosterols, containing 4 percent alcohol. The suggested dosage is 15 ml. immediately before each meal of medium size. The dose should be increased to 1½ or 2 tablespoonfuls when large or high fat meals are eaten. A total daily dose of 120 to 180 ml. (4 to 6 ounces) may be required in some individuals. To obtain optimum therapeutic effect, any food taken between meals should be preceded by a whole or fractional dose of Cytellin.

Delalutin

. . . an injectible progestational preparation, is now available from E. R. Squibb, division of Olin Mathieson Chemical Corp. It is a chemically 17-*alpha*-hydroxyprogesterone caproate dissolved in sesame oil with 30 percent benzyl benzoate. Conversion of the practically inert 17-*alpha*-hydroxyprogesterone with caproic acid to produce 17-*alpha*-hydroxyprogesterone-17-*n*-caproate not only considerably prolongs the duration, but greatly increases the potency and effectiveness of the compound. A single intramuscular injection of 250 mg. of Delalutin produces a progestational effect on the estrogen-stimulated endometrium that lasts approximately 14 days in most patients.

While the mechanism for the prolonged progestational action of Delalutin is not clear, the evidence indicates that as the compound is absorbed from the site of the injection or is metabolized, the caproate ester is not degraded to either free progesterone or the weakly progestational free 17-*alpha*-hydroxyprogesterone. It is thought that the compound is transported intact to the tissues in which it exerts its biologic activity and is slowly metabolized as it produces its action.

In pregnancy disorders such as habitual and threatened abortion Delalutin supplies enough progestational activity to approximate that present in normal pregnancy. It also makes possible a simplified economical treatment for normalizing the ovarian function in nonpregnant women. Other therapeutic uses of this compound include its beneficial effect in premenstrual tension, dysmenorrhea, and female infertility.

The usually effective therapeutic dose of Delalutin is 125 to 500 mg. as a single intramuscular injection every one to two weeks, depending upon the amount of estrogen that is exerting an effect during the Delalutin action, the condition that is being treated, and the clinical response of the patient. Delalutin is available in vials of 2 and 10 ml. Each ml. provides 125 mg. of 17-*alpha*-hydroxyprogesterone caproate. Vials of Delalutin should be stored at room temperature. Storage at low temperatures may result in the separation of some crystalline material which redissolves readily on warming to room temperature.

Demerol with Atropine

. . . solution for injection is available from Winthrop Laboratories. The preparation is supplied in 2 ml. ampuls, each ml. containing 50 mg. Demerol hydrochloride and 0.2 mg. (1/300 grain) atropine sulfate.

Demerol with Scopolamine

. . . solution for injection has been introduced by Winthrop Laboratories. The preparation is particularly useful for preoperative medication as well as for obstetric analgesia and amnesia. Each ml. of the solution for injection contains 50 mg. of Demerol hydrochloride and 0.2 mg. (1/300 grain) of scopolamine hydrobromide.

Demerol with scopolamine is administered by intramuscular or subcutaneous injection. Dosage ranges for preoperative use and in obstetrics are indicated in the literature.

Ecolid

. . . a new orally effective ganglionic blocker recommended for the treatment of the more severe forms of hypertension, is now supplied by Ciba Pharmaceutical Products, Inc. Following oral administration Ecolid elevates the threshold of the sympathetic and parasympathetic ganglion cells to acetylcholine liberated by the preganglionic fibers. The drop in blood pressure that follows results from suppression of the sympathetic vasoconstrictor reflexes transmitted to the extremities by the postganglionic fibers.

Advantages of Ecolid are its long action, rapid absorption, consistent and predictable response to oral administration, usual lack of severe gastrointestinal side effects, and the fact that treatment can be carried out on an outpatient basis with frequent observations.

Ecolid is recommended for treatment of moderate, severe, and malignant hypertension only. It should *not* be used in mild, labile hypertension.

Ecolid (chlorisondamine chloride Ciba) is a potent drug and it should be used with the same caution as other ganglionic blocking agents. It should not be utilized in patients with severe coronary insufficiency or recent myocardial infarction. It should be used cautiously in hypertension associated with the following: renal disease with a rising nonprotein nitrogen level; cerebral complications; encephalopathy; or pyloric stenosis. If constipation results, the dosage should be reduced until normal bowel function is restored by laxatives. Blurring of vision is the one side effect the incidence of which is as great or greater with Ecolid than with other ganglionic blockers. The patient should be warned against driving cars or operating machinery when such visual disturbances occur.

As with all ganglionic blockers, individualization of dosage is essential for optimal results. In ambulatory patients therapy with Ecolid should be initiated with a morning dose of 25 mg. On the second night the evening dose of 25 mg. should be started. Depending on response, the dosage may be increased at intervals thereafter by 25 mg. increments until the desired therapeutic effect is obtained. The average maintenance dosage is 50 to 100 mg. twice daily. For more rapid effect in hospitalized hyper-

tensives, an intensive therapeutic program may be put into effect. An initial dosage of 50 mg. twice daily may be given. Depending on the response the dosage may be increased by 50 mg. daily until optimal response is attained. During the first few days of therapy the patient should be kept in bed to avoid episodes of severe postural hypotension.

Ecolid is supplied as 25 mg. (ivory) and 50 mg. (pink) tablets in bottles of 100.

Flexin

. . . the first orally effective drug for the relief of muscle spasm in musculoskeletal and neurological disorders, has been developed by McNeil Laboratories, Inc. Unrelated to any available agents, it has never before been synthesized. The generic name is zoxazolamine and it is described as a "lissive" agent. That is, it reduces skeletal muscle spasm without interfering with normal muscle power or activity. Flexin is supplied in bottles of 50 scored yellow tablets of 250 mg. each.

Flexin is indicated for conditions whenever musculoskeletal spasm is present, such as low back pain, fibrositis, spondylitis and rheumatoid arthritis. It has also been found useful as an adjunct in the treatment of neurological disorders such as spinal spasticity states, cerebral palsy, multiple sclerosis, cerebral vascular accidents and Parkinson's disease.

Marked freedom from side effects has been observed in many patients, some of whom have undergone daily therapy for as long as twelve months. Moreover, the duration of action—approximately six hours—and the ease of maintenance dosage are emphasized.

Editor's Note: The description of Flexin which appeared in the March-April issue of The Bulletin contained a typographical error which implied an incorrect inference.

Florinef-S Ophthalmic

. . . an ophthalmic preparation containing fludrocortisone acetate, neomycin and gramicidin, has been announced by E. R. Squibb, division of Olin Mathieson Chemical Corp. This preparation has about 13 times the anti-inflammatory, anti-allergic potency of hydrocortisone. It is particularly useful in inflammatory eye disorders threatened by, or actually contaminated with secondary bacterial infection. Florinef-S Ophthalmic causes no toxic or allergic reactions and is well tolerated. The ophthalmic suspension contains 0.1 percent fludrocortisone acetate combined with 2.5 mg. neomycin and 0.025 mg. gramicidin per ml. of sterile aqueous vehicle, and is available in 5 ml. plastic dropper bottles. The ophthalmic ointment is the same strength and is supplied in Plastibase, a non-water-absorbing ointment base, in 3.6 Gm. tubes with ophthalmic tips.

Inversine

. . . a potent ganglionic blocking agent, is now available from Sharp & Dohme, division of Merck & Co., Inc. Inversine, a brand of mecamylamine hydrochloride, is unlike other antihypertensives in that it is completely absorbed following oral administration. Because of its complete absorption from the gastrointestinal tract, it offers excellent reproducibility and predictability; in a given patient, the same dose of Inversine elicits the same response time after time with minimal day-to-day fluctuation. Once patient titration has been accomplished, the hypertensive patient can be controlled smoothly, with predictable results, free of the erratic and often dangerous fluctuations in response which have heretofore constituted the major objective to ganglionic blockade.

Side effects of Inversine are substantially the same as those encountered with other ganglionic blocking agents. At the first sign of constipation vigorous treatment must be initiated immediately. Use of Inversine is contraindicated in coronary insufficiency, organic pyloric stenosis, and recent myocardial infarction.

The recommended initial dosage of Inversine is 2.5 mg. twice daily, preferably after meals. This may be increased by 2.5 mg. at intervals of no less than two days until desired response is obtained. In severe or urgent cases, the increments may have to be larger or more frequent, with the largest dose given preferably at noon or in the evening. The drug is extremely potent. It should always be titrated according to the individual patient's orthostatic blood pressure response.

Inversine is supplied as 2.5 mg. scored and 10 mg. quarter-scored tablets in bottles of 100.

Meti-Derm Cream

. . . is a formulation of the free alcohol of prednisolone (Meticortelone) in a water-washable base for local administration in all skin disorders responsive to topical corticosteroid therapy. More active at tissue level than topical hydrocortisone, milligram for milligram, Meti-Derm cream exerts pronounced anti-inflammatory, anti-allergic and antipruritic action at the site of the lesion with minimal risk of systemic effects such as sodium retention, edema and weight gain. It is indicated as an aid to conventional management of allergic dermatoses and is particularly valuable in contact dermatoses, in atopic dermatitis, and in nonspecific pruritus of anus, vulva, and scrotum. In many cases, suppression of allergic skin reations and severe itching may be complete. Also, Meti-Derm has been shown to be especially pleasing to patients because it is water-washable and cosmetically acceptable. Meti-Derm cream is a product of Schering Corporation.

Neo-Delta-Cortef

. . . 0.25 percent eye-ear drops, a sterile suspension of prednisolone acetate with neomycin sulfate, is now marketed by The Upjohn Company.

It is indicated for treatment of acute ocular inflammations and infections of the external ear. The usual dosage in ocular inflammations is 1 or 2 drops placed in the conjunctival sac every hour during the day and every two hours at night. In otitis externa, 2 or 3 drops may be placed in the external ear canal two or three times daily.

Each ml. of Neo-Delta-Cortef 0.25 percent eye-ear drops contains delta-1-hydrocortisone acetate, 2.5 mg. (0.25 percent); neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); preserved with myristyl-gamma-picolinium chloride, 1:5000. It is available in 5 ml. bottles with droppers.

Rhulispray

. . . a new spray-on preparation for the relief of itching and pain due to ivy and oak poisoning, hives, insect bites, and other minor skin irritations commonly occurring during the summer months, is now being marketed by Lederle Laboratories.

Available in a three-ounce aerosol dispenser, Rhulispray is sprayed directly on the affected areas. The preparation penetrates the skin quickly, dries rapidly, thus eliminating the danger of soiled or stained clothing.

The active ingredients of Rhulispray are: zirconium oxide 1 percent; menthol 0.009 percent; camphor 0.098 percent; calamine 0.98 percent; benzocaine 0.98 percent; and isopropyl alcohol 9.5 percent.

Serpatilin

. . . is a combination of Serpasil (reserpine) and Ritalin hydrochloride (methyl-phenidylacetate hydrochloride) available from Ciba Pharmaceutical Products, Inc. This combination of the tranquilizing drug Serpasil and the mild psychomotor stimulant Ritalin is complementary in action. Serpasil releases the individual from tension and anxiety, while Ritalin stimulates and brightens his mental outlook and thus tends to overcome the depressant and other undesirable side effects of Serpasil. Serpatilin is indicated for use in a wide variety of conditions including hypertension, in chronic fatigue and mild depressed states, vague psychosomatic complaints, menopausal ailments, mentally retarded patients, and in geriatric patients. A report on the use of Serpatilin appeared in the *J. Am. Med. Assoc.* Jan. 28, 1956.

Sparine

. . . a new potent ataractic drug for the management of the acutely agitated patient, is now available from Wyeth Laboratories. Sparine (promazine hydrochloride Wyeth) has been found to control effectively symptoms of central nervous system excitation, to allay apprehension and anxiety, and calm the acutely agitated patient. It should not be used in the treatment of chronic mental disturbances, but should be restricted to the control of periodic episodes of acute agitation occurring in such patients. It is indicated in the management of a variety of acute mental disturbances including such alcohol-induced syndromes as delirium tremens, acute hallucinosis, acute tremulousness and inebriation, as well as agitation due to various psychoses and withdrawal symptoms of drug addiction.

Side reactions following the short term use of Sparine have been few and not serious in nature or degree. The sedative effect is a desirable action under most circumstances; however, in certain cases the drug may cause undesirable drowsiness. This will usually disappear on continued therapy or can be controlled by decreasing the dose. Transitory postural hypotension has been noted in a few patients, usually following the first parenteral dose. When this happened, recovery was spontaneous and the symptoms of weakness and dizziness disappeared. Until greater experience is gained through wider use of Sparine, patients should be observed frequently and asked to report the sudden appearance of any signs of infection. As with any new and potent agent, if white blood cell counts and differential smears give an indication of severe cellular depression, the drug should be discontinued and antibiotic and other suitable therapy should be initiated.

Sparine should not be used in comatose states due to central nervous system depressants (alcohol, barbiturates, opiates, etc.). In patients with cerebral arteriosclerosis, coronary heart disease, or other conditions where a drop in blood pressure may be undesirable, Sparine should be used with caution. In these cases it may be helpful to follow the blood pressure for an hour or more after the initial dose.

The amount, route of administration, and frequency of dose should be governed by the degree of central nervous system excitation present and patient's response. In the management of acutely agitated patients, it is recommended that Sparine be given intravenously in initial doses of 50 to 150 mg. If the desired calming effect is not apparent within 5 to 10 minutes, additional doses up to a total of 300 mg. may be given. Once the desired effect is obtained it may then be given intramuscularly or orally in doses of 25 to 200 mg. at 4 to 6 hour intervals. The percentage of effective results does not appear to be materially affected by the administration of doses in excess of 800 mg. to 1000 mg. daily. It is therefore recommended that the total daily dose not exceed one gram (1000 mg.).

Sparine is supplied as tablets in the following strengths: 25 mg. (yellow): 50 mg. (orange); 100 mg. (pink); and 200 mg. (red); in bottles of 50 and 500 tablets. The injection is supplied in a strength of 50 mg. per ml. in vials of 2 and 10 ml.

Terrabon Suspension

. . . a new oral suspension employing Terramycin in the form of a special calcium salt has just been marketed as a stable, homogenized, peach-flavored liquid by Pfizer Laboratories, division of Chas. Pfizer & Co., Inc. This new suspension contains 125 mg. Terramycin activity (as calcium-dioxytetracycline) per 5 ml., and is recommended for treatment of the wide range of diseases against which Terramycin has proved effective both in children and adults.

Two sizes of Terrabon are available, 2 ounce and 1 pint bottles. The unusual flavor of the preparation, its convenience, and its long shelf life are the reasons for changing the Terramycin oral suspension formula.

Thora-Dex Tablets

. . . offer a combination of Thorazine (chlorpromazine) and Dexedrine (dextro-amphetamine sulfate). A product of Smith, Kline and French Laboratories, Thora-Dex Tablets are indicated in a wide variety of mental and emotional disturbances marked by anxiety, agitation, apprehension and depression; in somatic conditions complicated by emotional stress; and when Thorazine alone causes undesired drowsiness, that is in the treatment of nausea and vomiting in ambulatory cases.

Thora-Dex Tablets are available in two strengths: Thora-Dex Tablets (No. 1), each tablet containing Thorazine, 10 mg. and Dexedrine, 2 mg.; Thora-Dex Tablets (No. 2), each tablet containing Thorazine, 25 mg. and Dexedrine, 5 mg. Each strength is available in bottles of 50 and 500.

Ziradryl Lotion

. . . for the prevention and treatment of poison ivy and poison oak, has been introduced by Parke, Davis and Company.

Generous application of the lotion is recommended when contact with poison ivy or oak is anticipated. Cleansing of affected areas with soap or water and three to four applications of Ziradryl daily are suggested "as soon as possible" for skin areas unprotected at time of exposure. If inflammation and itching already have started, "Cautious treatment" and application of Ziradryl three to four times daily are recommended.

Impressions...

an American pharmacist in Europe

by GLENN SONNEDECKER, *Secretary, American Institute of the History of Pharmacy*

Fourth in a series of informal columns dispatched to THE BULLETIN by Dr. Sonnedecker during his year in Europe as a Fulbright Research Scholar and Fellow of the Guggenheim Foundation.

Society of Apothecaries

LONDON SEEMS DESERTED ON A SUNDAY. A feeble sun filters through light fog. I am looking for a distinguished hospital pharmacist in the cavernous Mansion House station of the underground (subway), from whence we shall go to the annual Master' Day church service of the Worshipful Society of Apothecaries. It was this Society that James I chartered in 1617 as the first separate organization of pharmacy in England.

Most readers may recall, however, that by the 18th century these apothecaries had become recognized as primarily general medical practitioners. The modern British chemist-and-druggist stems more directly from the "chemists" and the "druggists" who grew into the pharmaceutical role no longer firmly claimed by the apothecaries. Thus, today the Society of Apothecaries of London is a *medical* organization, which includes a few pharmacists on more or less an honorary basis. My host, T. Douglas Whittet, is one of them.

We make our way through the City to the Church of St. Mary (Anglican). In the stained glass windows handsome coats of arms testify to the patronage of various old guilds. I do not find the arms of the Society of Apothecaries among them; later learn that the church of the Society, St. James at Garlickhythe, was bombed out and is still undergoing restoration.

The Master's Day service, exclusively for members, rededicates them to their profession. After the benediction the Wardens, enrobed in their traditional livery, file out behind their new Master, Dr. Neville S. Finzi, bearded and old, encumbered by a heavy neck chain bearing the honored seal of his high office.

We now proceed to Apothecaries Hall in Blackfriar's Lane, which is abutted by Apothecaries Street. On the way we pass through Bucklesbury Lane, a crooked alley between Cheapside and Poultry, where drug dealers congregated in medieval times. But it no longer harbors a single drug dealer.

The present Apothecaries Hall arose in 1668 after the original building burned in the Great Fire; during the centuries, meanwhile, it has been considerably altered and remodeled. We enter through a paved courtyard (where there are still some fragments of a 13th century monastery), mount the handsomely carved staircase, and join the members over a glass of sherry in a richly paneled room. Soon comes the familiar cry of "Pray silence," from the toastmaster (not the American kind), who bids us into the magnificent Great Hall for the Master's Day luncheon. Here still hang long banners that the original apothecaries used to adorn their State Barge, which represented pharmacy in the procession down the Thames on Lord Mayor's Day and similar occasions.

The gracious custom of toasting following a social repast is here climaxed by the centuries old toast of the Master, to the greater fellowship and professional service of the members, ending with the words "until time shall cease." The members now lift their glasses, look into each others eyes, murmur "Until time shall cease," and drink.

Douglas Whittet and I now make our way through the crowd for a quick inspection of the Society's pharmaceutical antiques, then walk along Victoria Embankment, to part at the underground station. Whittet heads for University College Hospital, where he ably follows a long line of distinguished chief pharmacists (and apothecaries), such men as Ringer, Martindale, and Hampshire. I visited his pharmacy last week, where he presides over a staff of eleven pharmacists, soon to include a research assistant, and about an equal number of apprentices and other unlicensed personnel. They manufacture everything possible. One finds not only a modern sterile solution room and much power machinery, but also still in active use a crude-drug grinder, percolators and other extraction equipment.

CURRENT LITERATURE

edited by SISTER MARY ETHELDREDA, *St. Mary's Hospital, Brooklyn, N.Y.*

Hospital Management

HUNTER, JAMES A. and Associates: Hospital Medication Injection Costs, *Hosp. Management 81*:80 (Apr.) 1956.

Part II of a study of costs involved when medications are injected by the conventional syringe method and the costs involved when the disposable syringe method is used. Part II covers purchasing with a summary of the principal advantages claimed for the single dose closed systems along with observations made in the study. Includes schedule showing summary of costs per injection for specific medications. A concluding part of the study will be applied in determining the cost of medications given by the single dose closed system.

MORAVEC, DANIEL F.: A Preview of Things to Come, *Hosp. Management 81*:102 May (1956).

An analysis of the purpose of the pharmacy section in this publication and the approach the editor considers using to attain this goal.

Hospital Progress

SKOLAUT, MILTON W.: Trends Indicate Current Direction of Services in Hospital Pharmacies, *Hosp. Progress 37*:100 (Mar.) 1956.

Presents the numerous factors which are effecting or will affect the type of pharmacy service rendered in hospitals.

COMENS, PHILIP: Pharmacology of Hypotensive Drugs, *Hosp. Progress 37*:150 (May) 1956.

A review of the hypotensive drugs with particular reference to recent advances in this field. Pharmacology of some of the newer agents such as the Rauwolfia drugs, pentapyrrolidinium, and hydralazines is covered.

Hospitals, J.A.H.A.

CLAGUE, EWAN: Work Injuries to Hospital Employees, *Hospitals 30*: 37 (May 16) 1956.

One of a series of articles devoted to a detailed discussion of safety and the hospital. This presents a preliminary study of the Bureau of Labor Statistics showing the work injury experiences of hospital employees, based upon records for the year, 1953. It is noted from statistics that Pharmacy Departments account for an average of 2.8 disabling injuries per million hours worked, the average for the Professional Care Division being 7.6 disabling injuries per million hours worked. In the Professional Care Division, the record indicates that the greatest safety problems lie in four activities—nursing service, Physical Therapy, Occupational Therapy, and Clinical Laboratory Operations.

The Modern Hospital

NYHAN, WILLIAM L. and HENDERSON, WALTER J.: Radioactive Isotopes in Clinical Medicine, *Modern Hosp. 86*:104 (Apr.) 1956.

A comprehensive review of isotopic methods used in diagnosis and therapy.

WILLIAMS, HARRY L.: Newer Views on Thyroid Function, *Modern Hosp. 86*:104 (May) 1956.

A discussion of the trends in thought on the activity and function of the thyroid gland and the mode of action of antithyroid drugs.

Southern Hospitals

BARNETT, CHARLES B.: How, When and What of a Formulary, *South. Hosp. 24*:51 (Mar.) 1956.

A simple, straightforward delineation of the corrcet steps to take in preparing a formulary.

J. Am. Pharm. Assoc., Pract. Pharm. Ed.

WEINGOLD, WILLIAM L.: The New Official Drugs, Part I-U.S.P. XV, *J. Am. Pharm. Assoc., Pract. Pharm. Ed. 17*:156 (Mar.) 1956.

Includes complete listing of new preparations included in the new *Pharmacopeia* along with descriptions, category, dosages, commercial sources, and trade names.

WEINGOLD, WILLIAM L.: The New Official Drugs, Part II—N.F. X, *J. Am. Pharm. Assoc., Pract. Pharm. Ed. 17*:220 (Apr.) 1956.

A continuation of article starting in March issue, this one covering new preparations included in the new *National Formulary*.

American Professional Pharmacist

STEELE, FRANK J.: Smaller Hospitals Can Compound Products in Volume, *Am. Profess. Pharmacist 22*:236 (Mar.) 1956.

Presents the opportunities for bulk-compounding of preparations and ordinary items used in above-average quantities in a 200 bed hospital without the necessity of an elaborate program.

ZUGICH, JOHN J.: Relationship Between Hospitals and Community Pharmacists, *Am. Profess. Pharmacist* 22:344 (Apr.) 1956.

Discusses the opportunities for developing a higher standard of pharmaceutical service in smaller hospitals by the cooperation of the community or independent retail pharmacist.

ASHP affiliates

Southeastern Society

Miami Beach, Florida was the scene of the Annual Meeting of the Southeastern Society of Hospital Pharmacists held April 18-20, 1956, in conjunction with the 19th Annual Meeting of the Southeastern Hospital Conference. Approximately fifty pharmacists from the six states and visitors from several other states were present and participated in the Conference. Terry B. Nichols presided and addressed the opening session on Wednesday afternoon when the preliminary business was presented. A Round Table discussion moderated by Mr. Joe Vance, Administrator, South Highlands Infirmary, Birmingham, Ala., held a panel of experts composed of Dr. Charles C. Hillman, Associate Dean, School of Medicine and Coordinator of Medical Affairs Jackson Memorial Hospital, Miami, Fla.; Dr. Don Francke, Chief Pharmacist, University Hospital, Ann Arbor, Mich., Mr. Charles T. Harrell, Sales Manager, Bristol Laboratories, New York, N.Y. Those attending were presented a Banquet Wednesday evening in the Zodiac Room of the Delano Hotel.

Speakers on Thursday morning included Mr. Erwin Kastrup, Editor of *Facts and Comparisons,* St. Louis, Mo.; Dr. Randall B. Tinker, University of Florida, Gainesville, Fla.; and Mr. Vernon Trygstad, Director of Pharmacy Service, Department of Medicine and Surgery, V.A. Central Office, Washington, D.C. The program was followed by a Luncheon and Fashion Show in Burdine's Tea Room. A Report of Progress of the University of Miami Medical School, the reports of conference registration and the Society's Secretary and Treasurer comprised the Thursday afternoon program, followed by a tour of the University Research Farm. Dinner Thursday evening was at the Roney Plaza.

Breakfast at the Shore Club began Friday's program, followed by important talks and a business session. The nominating Committee, consisting of Mrs. Lillian Price, Mr. Albert P. Lauve and Miss Johnnie Crotwell, made the following report: *For President,* William W. Taylor and Perry E. Cox; *For Vice-President,* Malcolm F. Claus and Mary Wernersbach. *For Secretary-Treasurer*: James Mitchener and Howard D. Clem.

Oklahoma Society

Dr. Charles Schwartz, Professor of Pharmaceutical Chemistry, Southwestern State College in Weatherford, was the principal speaker at the April 19 meeting of the Oklahoma Society of Hospital Pharmacists. Discussing "Hypotensive Drugs," Dr. Schwartz classified them according to chemical composition and listed drugs currently used to treat hypertension. He noted the fact that the whole field of hypotensive drugs is in the stage of study and change and emphasized the importance for pharmacists to keep abreast of recent developments.

During the business session, plans were outlined for the May 9 meeting to be held in conjunction with the Convention of the State Pharmaceutical Association. Also, Sister Mary Teresa, President, reported in detail on actions taken at the ASHP Annual Meeting held in Detroit in April.

Florida Society

The Florida Society of Hospital Pharmacists has recently reorganized and Miss Mary Wernersbach, Mount Sinai Hospital, Miami Beach, has been elected President. The Secretary is Mrs. Jean Whitmore Poucher, St. Vincent's Hospital, Jacksonville.

Greater New York Chapter

"Anemias and Leukemias and Their Treatment," was the subject of a discussion at the February 21 meeting of the Greater New York Chapter of the ASHP. The speaker, Dr. L. J. Acierne, is a member of the Medical Staff at St. Peter's Hospital where the meeting was held. The discussion covered the various types of anemias and drugs being used in their treatment.

Northern California Society

Members of the Northern California Society of Hospital Pharmacists met at the Veterans Administration Hospital in Oakland on February 14. The program was presented by Mr. Anthony Gazzola, representing the State Bureau of Narcotic Enforcement. He showed a film on drug addition and discussed the problems covering enforcement of narcotic laws.

The meeting was presided over by President Marie Kuck who made committee appointments for the new year. Announcements included those on a one-day seminar on radioisotopes scheduled at the University of California and a two-day Seminar to be held in October.

Ohio Society

The Ohio Society of Hospital Pharmacists held its Annual Meeting on April 9, 10 and 11 in conjunction with the Annual Convention of the Ohio Hospital Association. Meetings were scheduled at the Franklin County Veterans Memorial Building and the Deshler-Hilton Hotel in Columbus.

The following papers were presented during the two-day meeting of the Ohio Society.

"Undergraduate Program for Hospital Pharmacy," by Dr. Robert Salisbury, Ohio State University, Columbus.

"Methods in a Hospital Pharmacy," by R. D. Wayland, Industrial Engineer, H. Lukens, Cleveland.

"Hospital Pharmacy — Gateway to Administration," by W. D. Cairns, Products Addition Studies Division, Eli Lilly and Company, Indianapolis.

"Personnel — Fad, Fact, or Fancy?" by Mary R. Hunt, Associate Director Student Personnel, Antioch College, Yellow Springs, Ohio.

"Workshop on Ideas for Improving Pharmacy Service."

"Medico-Legal Aspects of Hospitals," by Dr. George F. Archambault, Past President, AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Washington, D. C.

Illinois Chapter

The monthly meeting of the Illinois Society of Hospital Pharmacists was held at the St. Clair Hotel in Chicago on Tuesday Evening, March 13. Approximately 75 hospital pharmacists and friends attended the meeting which was sponsored by E. R. Squibb and Sons. The highlight of the meeting was a discussion by Dr. William Heller, Chairman of the ASHP Committee on Pharmacy and Pharmaceuticals. He presented the functions and plans for initiating the American Hospital Formulary Service and asked for cooperation of the hospital pharmacists and affiliated chapters.

New officers of the Illinois Chapter of the ASHP include President Morris Gordon, Vice-President Lewis A. Cooke, and Secretary-Treasurer Edward A. Hartshorn. Members of the Executive Council include Charles Lev, Albert Almond, and Florence Hatter.

The April meeting of the Illinois Chapter was held at Presbyterian Hospital in Chicago. The program included the following papers:

"Interviewing the Salesmen," by Lewis Cooke, St. Joseph Hospital, Chicago.

"Night Service," by William Cummings, Michael Reese Hospital, Chicago.

"Alcohol Regulation and Control,' by James Palmgren, Evanston Hospital Association, Evanston.

Maryland Society

The Maryland Association of Hospital Pharmacists met at the Kelly Memorial Building in Baltimore on March 27. Dr. John C. Krantz, Jr., Head of the Department of Pharmacology of the University of Maryland Medical School, was the principal speaker. He traced the development of anesthesia from its discovery to the present time. It was particularly interesting to hear Dr. Krantz relate his own experiences in the search for newer anesthetic agents.

A short business meeting followed in which the President, Dr. John A. Scigliano, was selected to represent the group at the ASHP Annual Meeting in Detroit.

Midwest Association of Sister Pharmacists

The Midwest Association of Sister Pharmacists met at St. Mary of Nazareth Hospital in Chicago on April 19. Papers scheduled for presentation included the following:

"Today's Trend in Ophthalmology," by Dr. L. H. Lassiter, Instructor in Ophthalmology at the University of Illinois.

"Pharmacology of New Drugs," by Sister Mary John, O.S.F.

Sister M. Tarcisia, O.S.F., also presented a report on the history of the Midwest Association.

Western Pennsylvania Society

"Narcotic Control in Hospitals," was the subject of a panel discussion at the March 15 meeting of the Western Pennsylvania Society of Hospital Pharmacists. Participants included Mr. Italo Bianculli who discussed methods of control in VA Hospitals, and Miss Kathleen Hvozdovich who presented methods used in civilian hospitals and pointing out the recommendations and interpretations published by the ASHP Committee on Narcotic Regulations. As a special guest, Mr. Rex McKay, the pharmaceutical representative for McKesson and Robbins, Co., Pittsburgh, described the processes of handling a typical order for narcotics through the wholesaler.

At the April 19 meeting of the Western Pennsylvania Society, Mr. Darrell L. Gifford, Manager, Technical Sales Division, American Sterilizer Company, discussed "Why the Hospital Pharmacist Should Make Intravenous Solutions." Mr. Gifford pointed out that the compounding of solutions for intravenous use is not difficult and can be a source of great savings to the hospital.

Oregon Society

A joint meeting with a group of laboratory technicians was sponsored by the Oregon Society of Hospital Pharmacists on April 11. The meeting was held at St. Vincent's Hospital in Portland.

During the business session, plans were made for including a page for hospital pharmacists in the *Oregon Pharmacist* and participation in the Pharmacy Section of the Convention of the Association of Western Hospitals being held in Seattle in April.

Western New York Chapter

Dr. George F. Archambault, Chief of the Pharmacy Branch, Division of Hospitals, U. S. Public Health Service, was the guest speaker at the April 15 meeting of the Western New York Chapter of the ASHP. Dr. Archambault spoke on "The Law of Hospital Pharmacy."

Philadelphia Hospital Pharmacists' Association

More than one hundred members participated in the March meeting of the Philadelphia Hospital Pharmacists' Association which was scheduled in two sections so that all members would have an opportunity to attend either in the afternoon or evening. A dinner sponsored by E. R. Squibb and Sons was scheduled between the two sessions.

Highlighting the meeting was a discussion on the activities of the ASHP Committee on Pharmacy and Pharmaceuticals by Dr. William Heller, Chairman. Mr. Russell Zimmerman, Sales Manager of Squibb's Special Projects Division spoke also on the possible contributions of industry to the American Hospital Formulary Service.

New members of the Philadelphia Association introduced at this meeting included William Bartlett, Memorial Hospital, Wilmington, Del.; William R. Zeglin, Presbyterian Hospital, Philadelphia; Harry N. Kaplan, relief hospital pharmacist; Sister Mary Irenus Matthews, St. Joseph's Hospital, Reading; and Zeldia Blatman, Graduate Hospital, Philadelphia.

Massachusetts Society

The March 28 meeting of the Massachusetts Society of Hospital Pharmacists was held at the Hotel Statler in Boston in conjunction with a dinner sponsored by Ciba Company. Business transacted in-

cluded a report of the committee appointed to look into inequities in salaries for pharmacists in city and state institutions; the possibility of having a Pharmacy Section at the New England Hospital Assembly, election of officers, and a report on the vote to amend the Society's Constitution and By-Laws.

New officers of the Massachusetts Society are President Charles Schraub, New England Deaconess Hospital, Boston; Vice-President William Grady, Worcester Memorial Hospital, Worcester; and Secretary-Treasurer Thelma C. Lezberg, Massachusetts General Hospital, Boston.

Southeastern New York State Chapter

Hospital pharmacists in the New York City Area have formed an organization and have expressed an interest in affiliating with the ASHP. The first meeting of the group was held on January 12 at the Lenox Hill Hospital in New York City. Participation in the activities of the chapter is sought from all pharmacists who are actively engaged in the practice of hospital pharmacy. Meetings and programs are being planned which will be of practical interest to pharmacists engaged in hospital or clinic practice, and also those in educational or administrative positions.

At the first meeting a Constitution was adopted and officers were elected. Mr. Harold Neham, VA Regional Office, New York City, is serving as President of the new Chapter. Other officers are Vice President Goldie Goldman, Maimonides Hospital of Brooklyn, Brooklyn, N. Y.; Secretary Leo Blackman, Mount Sinai Hospital, New York City; and Treasurer Robert Bogash, Lenox Hill Hospital, New York City.

The first program of the Chapter was held on February 16 in the Lexington Hotel. The topic of discussion was "Formulary—Friend or Foe?" with Seymour B. Jeffries, Director of Pharmacy Administration, Brooklyn College of Pharmacy, serving as moderator of the panel. Participants on the panel included Dr. George Archambault, Director of Pharmacy Service, U. S. Public Health Service, Washington, D. C.; Mr. E. Burns Geiger, Hospital Sales Manager, Chas. Pfizer and Company, Brooklyn; Dr. Frederick Lascoff, Retail Prescription Pharmacist, New York City; and Mr. Frank Walton, Purchasing Agent of the New York Hospital-Cornell Medical School.

Greater Kansas City Society

A business meeting of the Hospital Pharmacists' Association of Greater Kansas City was held at the Menorah Medical Center on March 13 with thirty-five members and guests present. The guest speaker was Mr. Darrell Gifford of the American Sterilizer Company who discussed the preparation of intravenous solutions by the hospital pharmacist.

During the business session, plans were announced for the Hospital Pharmacists' Section of the Midwest Hospital Convention held in Kansas City on April 25-27. Also, the group voted to make a contribution to the A.Ph.A. Building Fund and individual members were urged to give toward this worthy cause.

A film on Sparine was shown by a representative of Wyeth Laboratories at the April 10 meeting of the Greater Kansas City Society. The group met at the Queen of the World Hospital during the afternoon.

Rochester Area Society

Members of the Rochester Area Society have developed plans for a project for the Fall to cover pharmaceutical calculations, buffered and isotonic solutions, milliequivalents, etc. Miss Alvina Morse will coordinate the program.

The Seminar on Sterilization continued at the February 13 and March 12 meetings with discussions covering the "History of Sterilization," by Paul Miller and "General Considerations and Methods," by Phil Teischer. Other talks on this subject scheduled include equipment and stoppers, cleaning and filtration, pyrogens, sterilization techniques, and bacteriostatic agents.

Akron Area Society

Dr. L. A. Gess, formerly a medical missionary to Nigeria, Africa, was the principal speaker at the March 14 meeting of the Akron Area Society. Over fifty persons attended including representatives of pharmaceutical companies who were invited as guests. The meeting was held at the Akron General Hospital. On welcoming the guests, Mrs. Jeanne Sickafoose, President, gave a brief outline of the purpose of the organization and special projects undertaken.

Following the meeting, Mr. William McElroy, Chief Pharmacist, led a tour of the new Pharmacy Department.

North Carolina Society

Mr. A. J. Darling, President of the North Carolina Society, has issued a listing of the committees for the year along with a brief statement covering the duties of each. This will serve as a guide for the entire membership and will contribute much toward promoting the state activities during the coming year.

Northeastern New York Society

"Teamwork Between Hospital Pharmacists and Detail Men," was the subject presented by Mr. Irving Rubin at a recent meeting of the Northeastern New York Society of Hospital Pharmacists. Mr. Rubin is Managing Editor on Pharmacy of the *American Druggist* and Editorial Director of the *American Druggist Blue Book*. In presenting his talk, Mr. Rubin outlined specific ways in which hospital pharmacists and medical service representatives can work together. The meeting was held on March 22 in Latham, N. Y. in conjunction with the Medical Representative Society of the Capitol District. Seventy-five people attended.

Washington State Hospital Pharmacists

Dr. Brock Chisholm, Past Director General of the World Health Organization, was the principal speaker at a joint meeting of the Washington State Hospital Pharmacists and the Puget Sound Branch of the A.Ph.A. held on February 13. The meeting took place at the Health Sciences Building on the University of Washington campus.

A current project of the group has been planning the program for the Pharmacy Section of the Association of Western Hospitals Convention held in Seattle April 23-26. Mr. Joe Birmingham is Chairman of the Pharmacy Section and Robarts Proper is the Program Chairman.

as the president sees it

PAUL PARKER
American Pharmaceutical Association, Washington, D. C.

Perhaps every new president envisions goals that are beyond accomplishment in one short year, yet when we review our achievements in the SOCIETY, it must have been this sort of dreaming that led to such remarkable progress.

The area of activity that particularly concerns me is that of affiliated chapters. *How can we provide the opportunity for a maximum number of hospital pharmacists to participate effectively in professional organizational work on the local level?* We now have forty-five affiliated chapters and still it is necessary for some people to travel very long distances to attend meetings. This makes it difficult for these people to attend regularly, to develop a continuing interest in the programs and to maintain an active interest in ASHP work. A possible solution would be to organize more and more affiliated chapters, giving attention to the matter of geographical overlapping. Increasing the number of chapters with a small membership potential expands the problem of financing, particularly to send delegates to the national convention. On the other hand, such groups are conducive to more discussion of practical problems, and thus might have a greater influence on improving the practice of pharmacy in the hospitals represented.

A second approach might be to organize affiliates of the affiliates. In other words, have state or regional groups which meet two or three times a year to coordinate the activity of a number of smaller groups within that state or region. This has the disadvantage of increasing the number of organizations to which the individual must contribute and also adds to the complexity of naming delegates to the national convention. According to the By-Laws, the affiliated chapters are entitled to one delegate for each additional fifty members. This does not consider the matter of overlapping of membership. For instance, I believe we now have delegates from regional chapters. The number of such delegates is based upon the number of members. These same members are counted again in ascertaining the number of delegates for the local chapter. There is nothing wrong with this system at the present time because the House of Delegates is almost never faced with an issue which requires a vote. We hope that at some future date this situation will be corrected. If the matter of representation from the affiliates is properly established, it will be easier to improve the activity of the House of Delegates when the time comes.

Perhaps the best answer would be to organize state or regional chapters which would be affiliated with the national organization; then local groups which would in turn be affiliated with the state or regional chapter. It would then become necessary to have delegates from the regional groups or the local groups, but not both. The former would probably be better.

Among the advantages for this type of structure we could list—a fair representation in the House of Delegates; a medium for implementation of policies both up and down the scheme of organization; better facility for individual participation; opportunity for broader programming at the regional level (such as seminars, institutes, etc.); and the opportunity for development of individuals for organizational activity. Disadvantages would include lack of fair representation of local groups if there were laxity in regional organization; increased complexity of organization; increased expense in some respects.

Certainly these thoughts have not been considered by any official group of the SOCIETY, but are ideas which can be classified only "as the president sees it."

Paul F. Parker

NEWS

Hospital Pharmacist Nominated to A.Ph.A. Post

MR. GROVER C. BOWLES, Chief Pharmacist at Baptist Memorial Hospital in Memphis, Tenn., has been nominated for a three-year term on the Council of the American Pharmaceutical Association. Mr. Bowles is a past-president of the SOCIETY and is well known in the pharmaceutical field. He has represented the ASHP in the A.Ph.A. House of Delegates for a three-year term and has actively participated in A.Ph.A. as well as SOCIETY affairs. *Hospital pharmacists are urged to vote in the A.Ph.A. election to assure representation of hospital pharmacy on the Council of the A.Ph.A.* Another hospital pharmacist, Dr. George F. Archambault who is also a Past President of the SOCIETY, is now serving a three-year term on the Council.

Nominations for officers and council members of the A.Ph.A. were made at the Convention in Detroit. All active members of the Association will receive ballots which must be returned within thirty days of the date printed on the ballot.

A complete list of the nominees for officers of the A.Ph.A. appears in the May issue of the Practical Pharmacy Edition of the *J. Am. Pharm. Assoc.*

Parker Appointed Director of Division

MR. PAUL PARKER has been appointed full-time Director of the Division of Hospital Pharmacy of the A.Ph.A. and the ASHP. He began his new duties at the Headquarters Building of the A.Ph.A. in Washington on May 1. Prior to his appointment Parker was with the University of Chicago Clinics, where he served as Chief Pharmacist since 1952.

Mr. Parker, currently President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, comes to the Division with the training and education of a career hospital pharmacist. He is a graduate of the University of Michigan having completed his undergraduate work in pharmacy in 1949 and the graduate program in hospital pharmacy in 1951. He received a Certificate of Internship in Hospital Pharmacy from the University of Michigan Hospital in 1951. Parker has also attended business college in Chillicothe, Mo. and served in the U. S. Navy from 1943 to 1945.

Mr. Parker has been active in the ASHP having served as a member of the Executive Committee, Chairman of the Committee on Program and Public Relations, Chairman of the Special Projects Committee, and as a member of numerous other committees. He has also contributed to THE BULLETIN and has been on the Editorial Staff for several years.

Mr. Parker has also been active in the Chicago Branch of the A.Ph.A. and served as its Secretary-Treasurer and Delegate to the A.Ph.A. House of Delegates. He was also Vice-President of the Illinois Chapter of the ASHP. Parker is also a member of the American Institute of the History of Pharmacy.

In assuming his new post Mr. Parker has taken over the functions discharged previously by Dr. Don E. Francke who served as part-time Director of the Division since 1949 and Gloria Niemeyer Francke who had been Assistant Director since 1947. Mrs. Francke, now residing in Ann Arbor, Michigan will continue her duties as Secretary of the SOCIETY.

1956 Whitney Lecture Award

Dr. George F. Archambault, Chief of the Pharmacy Branch, Division of Hospitals, U.S. Public Health Service, Washington, D. C., was the recipient of the 1956 H.A.K. Whitney Lecture Award. The Award, established in honor of the first chairman of the SOCIETY, is presented annually by the Michigan Society to an individual who has made outstanding contributions in the field of hospital pharmacy. This year for the first time, the event was held in conjunction with the ASHP Annual Meeting with leaders in the pharmacy and hospital fields participating. More than 250 persons attended representing all parts of the country. The event was held at the Hotel Statler in Detroit on April 9.

Dr. Archambault is a Charter Member of the SOCIETY and served as President during the 1954-1955 term. He is well known in the pharmaceutical

field and is the author of many papers in the field of hospital pharmacy administration and jurisprudence as well as the author of a Chapter on Hospital Pharmacy Administration in a textbook known as *Pharmaceutical Compounding and Dispensing* by Lyman and Sprowls.

Lederle Research Grant To ASHP

A $10,000 research grant made available to the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS by Lederle Laboratories Division of the American Cyanamid Co. was announced at the annual meeting of the ASHP in Detroit.

Monies from this grant will be allocated for research for the improvement of hospital pharmacy services and for the formulation and development of pharmaceuticals prepared in hospital pharmacies.

Administering this grant will be the SOCIETY's newly organized Committee on Research and Development to which President Paul Parker has named Milton Skolaut, Chairman, and Clifton Latiolais and William Heller. Research projects to receive support from this grant will be chosen by an independent Board of Selection composed of persons thoroughly familiar with hospital pharmacy and hospital pharmacy education.

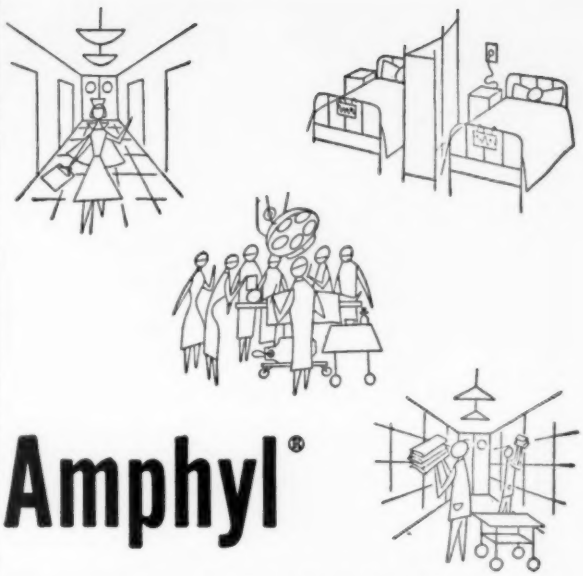
Proposals may be submitted by practicing hospital pharmacists, students, teachers, and others interested in the betterment of hospital practices. Application blanks will be available soon from the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, 2215 Constitution Ave., N.W., Washington 7, D. C. Receipt of all applications will be acknowledged.

Although no specific deadline for applications has been set, it would be desirable to submit applications as early as possible. All projects supported by the Lederle Grant must be processed, chosen by the Board of Selection, and submitted for final approval to the Executive Committee of the SOCIETY at its interim meeting, probably in November. Later applications may be eligible for possible future grants.

Teachers' Seminar Announced

The program and speakers for the eighth Annual Teachers' Seminar sponsored by the American Association of College of Pharmacy and supported by the American Foundation for Pharmaceutical Education have been announced. The Seminar this year is devoted to the subject of Pharmacy Administration. It is being held Sunday, July 22, through Friday, July 27, at The University of Texas College of Pharmacy.

The faculty for the Seminar is drawn from nine-



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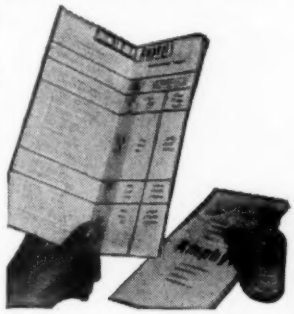
1. Klarmann, E. G.; Wright, E. S., and Shternov, V. A.: Applied Microbiology 1:19 (Jan.) 1953.



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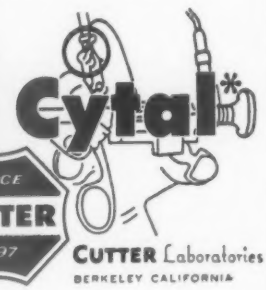

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†Schulte, et al., "Clinical Use of Cytal in Urology," Jrnl. of Urology, May 1954.

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The program is devoted to four major areas of instruction and graduate training. The four major areas are accounting, marketing, management and jurisprudence; one area is scheduled daily, with an open session in the morning followed by three workshops in the afternoon devoted to objectives and curriculum construction, methods of teaching and examining, and in-service activities; the study of graduate instruction is concerned with general requirements for graduate programs, educational resources, problems of graduate program development, faculty and personnel requirements.

The Seminar Committee is composed of Dr. Henry M. Burlage, Chairman, The University of Texas College of Pharmacy; Dr. R. A. Deno, University of Michigan College of Pharmacy; Dr. Louis C. Zopf, State University of Iowa, College of Pharmacy; Dr. Stephen Wilson, Wayne University College of Pharmacy; Mrs. Esther J. W. Hall, The University of Texas College of Pharmacy; Ex-Officio, Dr. A. Hamilton Chute, College of Business Administration, The University of Texas; and J. H. Arnette, Division of Extension, College of Pharmacy The University of Texas.

Pharmacist Speaks at Dental Society Meeting

MR. E. J. MARTIN, Chief Pharmacist at St. John's Hospital, Springfield, Mo., recently presented a lecture on "Prescription Writing" to the Springfield Dental Society. It was well received and plans have been made for future lectures on this vital subject.

Mr. Martin was with the U. S. Public Health Service prior to accepting his present position at St. John's. He plans to open a professional store in Springfield on July 1.

Parenteral Products Course Offered

The Philadelphia College of Pharmacy and Science and the Philadelphia Hospital Pharmacists' Association have announced plans for a special course on Parenteral Products during a two-week period beginning June 18. Recognizing that the preparation of parenteral products is an essential aspect of the modern practice of hospital pharmacy, the course is being offered to hospital pharmacists throughout the nation. The course, which is being conducted by Professor Kenneth E. Avis of the College Faculty, will include laboratory experiments, lectures, film showings, and demonstrations.

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there are additional requests, announcement has been made for another course to be offered from August 6 to August 17.

Pfizer Sponsors Seminar

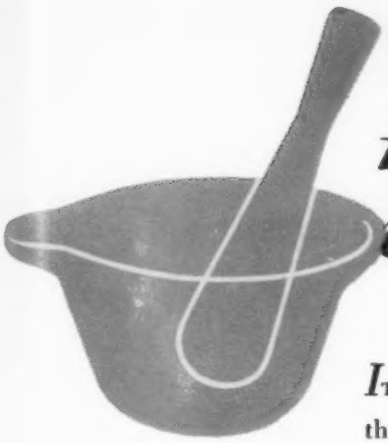
Pfizer Laboratories, in cooperation with the University of Maryland School of Pharmacy and the Maryland Association of Hospital Pharmacists, is sponsoring a one day Hospital Pharmacy Seminar in Baltimore, Maryland on Saturday, June 30, 1956. All hospital pharmacists in the area are invited to attend. The program has been scheduled for Saturday to permit hospital pharmacists to attend the Seminar with a minimum of inconvenience to their hospitals. Meetings will be held at the Kelly Memorial Building in Baltimore.

Moderator for the Seminar will be Dr. W. Arthur Purdum, Chief Pharmacist of Johns Hopkins Hospital. Other members of the Seminar faculty include Dean Noel Foss and Professor C. T. Ichniowski of the University of Maryland College of Pharmacy; ASHP President Paul Parker; A.Ph.A. Council Candidate Grover C. Bowles; Dr. John Scigliano, Assistant Chief Pharmacist of the National Institutes of Health; Mr. Francis S. Balassone, Chief of the Division of Drug Control, Maryland State Health Department; Mr. E. Burns Geiger and Mr. Paul Sullivan of Pfizer Laboratories; Mr. John Gooch, Assistant Director of Pharmacy Service of the V.A.; and Dr. R. A. Nelson, Director of Johns Hopkins Hospital.

Heinz Receives Lascoff Award

Mr. John B. Heinz, President of the American Pharmaceutical Association during the 1955-1956 term, was the recipient of the 1956 J. Leon Lascoff Memorial Award for his outstanding contributions to the pharmacy profession. The Award, named after a former president of the A.Ph.A., is presented annually by the American College of Apothecaries. The presentation was made by Mearl D. Pritchard, President of the College at the Annual Meeting in Detroit.

Mr. Heinz is from Salt Lake City, Utah where he operates a professional store. He is a former president of the American College of Apothecaries and of the Utah State Board of Pharmacy. Mr. Heinz is an Associate Member of the American Society of Hospital Pharmacists.



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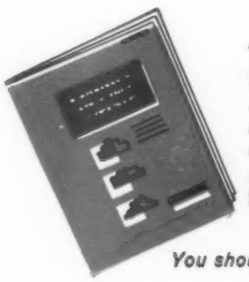

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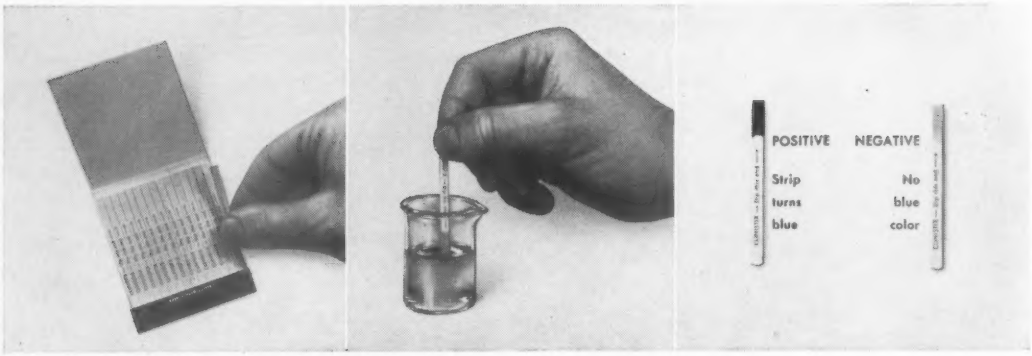

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1. Spies, T. D., et al.: GP 12:73, No. 1, 1955. 2. Boland, E. W.: J.A.M.A. 160:613, 1956. 3. Gillhespy, R. O.: Lancet 2:1393, 1955.

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MAY 1, 1956

The following ASHP members have sponsored the New Members listed on this page. The officers of the SOCIETY *and the Committee on Membership and Organization appreciate the efforts of the individuals who have encouraged New Members to join the national organizations. Sponsors will be listed along with the New Members in each issue of* THE BULLETIN.

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Bowles, Mary L.
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Schurman, John R., 9230 S. Hamlin Ave., Evergreen Park
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Torralba, Lydia F., 5479 S. Greenwood, Chicago
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POSITION as chief pharmacist in or within commuting distance of Philadelphia, preferably in hospital of 200-400 beds. Experience in both private and government hospitals in all phases of hospital pharmacy. Write to Mr. Harry Phaff, 1868 Commonwealth Ave., Brighton 35, Mass.

REGISTERED woman pharmacist (Grad. '52) who has three years' experience in a large teaching institution desires position as chief or assistant in hospital located in a South Central state. For further information write to the Division of Hospital Pharmacy, 2215 Constitution Ave., N.W., Washington 7, D. C. (PW-1).

WOMAN PHARMACIST, graduate of Philadelphia College of Pharmacy and Science (1956), desires position in hospital pharmacy preferably in Philadelphia area. Now working in hospital pharmacy as part of student training in hospital pharmacy course. Available July 1956. Address replies to Miss Kay Promish, 4033 Walnut St., Philadelphia, Pa.

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SUMMER WORK in hospital pharmacy in New York or New Jersey desired by student Brooklyn College of Pharmacy; four years' pharmacy experience. For additional information contact Gary M. Matoren, 1310 Grant Ave., Bronx 56, N. Y.

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The following openings in hospital pharmacy appeared in current issues of hospital publications. Anyone interested in the positions should write directly to the Agency indicated. A fee is charged when positions are secured through the services of a personnel agency.

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